UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF NORTH CAROLINA
CHARLOTTE DIVISION
CIVIL ACTION NO. 3:12-CV-213-MOC-DCK

CAMERON MCINTYRE,	)
	)
Plaintiff,	)
	)
vs.	)
	)
CHELSEA THERAPEUTICS INTERNATIONAL, LTD., et al.,	)
	)
Defendants.	)
	)

THIRD AMENDED CLASS ACTION COMPLAINT

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TABLE OF DEFINED TERMS

Term	Definition
Advisory Committee	Cardiovascular and Renal Drugs Advisory Committee
Advisory Committee Meeting	February 23, 2012 Meeting of the Cardiovascular and Renal Drugs Advisory Committee
CEO	Chief Executive Officer
Chelsea	Chelsea Therapeutics International, Ltd.
Class Period	September 20, 2010 through and including May 21, 2012
CMO	Chief Medical Officer
Company	Chelsea Therapeutics International, Ltd.
CRL	Complete Response Letter
DβH Deficiency	Dopamine Beta Hydroxylase Deficiency
Defendants	Chelsea Therapeutics International, Ltd., Simon Pedder, and William D. Schwieterman
Exchange Act	The Securities Exchange Act of 1934
FDA	United States Food and Drug Administration
FDCA	Federal Food, Drug, and Cosmetic Act of 1962
FDA Briefing Document	FDA Briefing Document for the Cardiovascular Renal Drugs Advisory Committee (CRDAC) published on February 21, 2012
Format Guidance	Guideline for the Format and Content of the Clinical and Statistical Sections of an Application
Hewitt	L. Arthur Hewitt, the Vice President of Drug Development and later the Chief Scientific Officer of Chelsea
IND	Investigational New Drug Application
Individual Defendants	Simon Pedder and William D. Schwieterman

Lundbeck	H. Lundbeck A/S
MSA	Multiple System Atrophy
NDA	New Drug Application
NDAN	Non-Diabetic Autonomic Neuropathy
OHQ	Orthostatic Hypotension Questionnaire
NOH	Neurogenic Orthostatic Hypotension
OH	Orthostatic Hypotension
OHDAS	Orthostatic Hypotension Daily Activity Scale
OHSA	Orthostatic Hypotension Symptom Assessment
PAF	Pure Autonomic Failure
PD	Parkinson's Disease
Pedder	Simon Pedder, Chelsea President and CEO of Chelsea
Plaintiff	Lead Plaintiff Roman Zak
SBP	Systolic Blood Pressure
Schweiterman	William D. Schwieterman, Vice President and CMO of Chelsea
SEC	United States Securities and Exchange Commission
SPA	Special Protocol Assessment
Zak	Lead Plaintiff Roman Zak

GLOSSARY

Term	Definition
Benefit-Risk Analysis	The balance between the therapeutic efficacy and safety risks imposed by a drug.
Dose Titration	The process of gradually adjusting the dose of medication until the optimal response is achieved.
Double-Blind Trial	A clinical trial in which neither the researchers nor the patients know which treatment is being administered.
Endpoint	The outcome that a clinical trial is designed to measure.
False Positive	A result that appears to indicate that a drug is effective but in reality is the result of mere chance.
Investigational New Drug Application	The vehicle through which drug sponsors formally request authorization from the FDA to test an unapproved drug on human subjects.
New Drug Application	The vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S.
Open-Label Trial	A clinical trial in which both the researchers and the patients know which treatment is being administered.
P-Value	The statistical probability of the occurrence of a given finding by chance alone in comparison with the known distribution of possible findings.
Pivotal Trial	A clinical trial intended to provide evidence of drug efficacy and supporting marketing approval by the FDA.
Primary Endpoint	The outcome that is the most important question being asked by the trial.
Statistical Significance	The likelihood that a result or relationship is caused by something other than mere random chance.

The allegations in this Third Amended Class Action Complaint are based on the personal knowledge of Lead Plaintiff Roman Zak ("**Zak**" or "**Plaintiff**") as to Plaintiff's own acts, and are based upon information and belief as to all other matters alleged herein. Plaintiff's information and belief is based upon the investigation by Plaintiff's counsel into the facts and circumstances alleged herein, including, without limitation: (i) review and analysis of those public filings Chelsea Therapeutics International Ltd. ("**Chelsea**" or the "**Company**") made with the United States Securities and Exchange Commission ("**SEC**") referenced herein; (ii) review and analysis of those press releases, analyst reports, public statements, news articles and other publications disseminated by or concerning Chelsea and the other defendants named herein (together with Chelsea, "**Defendants**") referenced herein; (iii) review and analysis of those Company conference calls, press conferences, and related statements and materials referenced herein; and (iv) review and analysis of those documents provided to Plaintiff or made publicly available by the United States Food and Drug Administration ("**FDA**") referenced herein. Many additional facts supporting the allegations herein are known only to Defendants and/or are within their exclusive custody or control and/or in the custody and control of the FDA. Plaintiff believes that additional evidentiary support for the allegations herein will emerge after a reasonable opportunity to conduct discovery.

NATURE OF THE ACTION

1. This is a federal class action on behalf of investors who purchased or otherwise acquired publicly traded Chelsea common stock between September 20, 2010 and May 21, 2012, inclusive (the "**Class Period**"), pursuing remedies under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 (the "**Exchange Act**") and Rule 10b-5 promulgated thereunder. These claims are asserted against Chelsea and certain of its officers and directors who, during the

Class Period, made materially false or misleading statements or omissions in press releases, analyst conference calls, and presentations, and filings with the SEC, *inter alia*, employed devices, schemes, and artifices to defraud, and engaged in acts, practices, and a course of conduct that operated as a fraud or deceit upon Plaintiff and other members of the Class.

2. In particular, Defendants misled investors regarding Chelsea's communications with the FDA, the results of Chelsea's only successful Phase III trial, and the strength of Chelsea's New Drug Application ("**NDA**") in light of the FDA's recommendation that Chelsea submit evidence of efficacy from two trials and durability of effect.

3. In order for a new drug to be approved by the FDA, the drug's sponsor must present "substantial evidence" of the drug's efficacy and safety. *See* 21 U.S.C. § 355(d). Typically, this evidence comes in the form of at least two adequate and well-controlled studies, each with a "p-value" below a pre-determined significance level, typically 0.05, demonstrating that the results are not likely to be the result of a false positive.[1] None of these requirements were news to the market or to Chelsea, which, during the Class Period, was attempting to secure FDA approval of droxidopa a/k/a Northera™, an orally-active synthetic precursor of norepinephrine for treatment of symptomatic neurogenic orthostatic hypotension ("**NOH**").

4. In fact, starting in 2007, in at least five meetings and 2 information letters, the FDA repeatedly "provided clear and consistent advice" to Chelsea "that 2 studies showing effectiveness, each with a p-value <0.05, were expected, that a single study *could* be adequate if the p-value was approximately 0.00125." Ex. A at 4, Office Director Decisional Memo from Ellis F. Unger, M.D., Acting Director of the Office of Drug Evaluation-I, FDA to Chelsea

[1] A "p-value" is the statistical probability of the occurrence of a given finding by chance alone in comparison with the known distribution of possible findings. For a more detailed discussion of p-values, see ¶32.

(March 28, 2012).[2] Additionally, the FDA made clear that "providing evidence of durability of effect . . . would be important." *Id.* Gathering long-term data showing effectiveness or an extended period of time was especially important for approval of droxidopa because "NOH represents a set of chronic diseases[.]" *Id.* at 18.

5. With these express requirements in mind, Chelsea devised a series of clinical trials whose purpose was to gather sufficient data to support a successful NDA for droxidopa. Initially, Chelsea developed its trial program to conform with the FDA's requests: Studies 302 and 301 were pivotal Phase III trials designed to demonstrate the safety and efficacy of droxidopa, and Study 303 was a three-month extension trial designed to provide evidence of the durability of droxidopa's effect.

6. Unfortunately for Chelsea, things did not go as planned. First, Study 302 failed to meet its primary endpoint. In light of prior FDA communications, Chelsea then had to switch gears. Chelsea scoured the data from Study 302 in an attempt to locate any positive results that it could use as a lifeline to keep Northera's clinical trials going. This after-the-fact analysis revealed that subjects experienced a nominally statistically significant improvement in the Orthostatic Hypotension Questionnaire ("**OHQ**") composite score. As a result, in November 2009, Chelsea sought permission from the FDA to change the primary endpoint of Study 301 from Item 1 of the Orthostatic Hypotension Symptom Assessment ("**OHSA**")—the same endpoint that Study 302 failed to meet—to the relative improvement in the OHQ composite score. The FDA agreed to this change to Study 301, but it warned that Chelsea would need to conduct an additional pivotal study because failed Study 302 could not be used as one of the two

[2] All citations are omitted and emphases are added unless otherwise noted.

efficacy trials required to support an NDA. In response, Chelsea proposed the initiation of a fourth trial, Study 306, to serve as a confirmatory efficacy study for its NDA.

7. Several months later, Study 301 was completed and purportedly met its amended endpoint with a statistically significant p-value of 0.003. But, as Chelsea recognized, the results appeared too good to be true: one testing center in Ukraine, Site 507, disproportionately contributed to the results of the study, such that it was the sole reason the study's results were statistically significant.

8. In yet another blow to the clinical program, Study 303 failed to meet its primary endpoint. Faced with failed Study 302, questionable results from Study 301, no evidence of durability of effect, a history of failing to ever generate product revenues, and a going concern letter from the Company's auditors, Defendants devised a fraudulent scheme to deceive the FDA and investors alike in an effort to obtain FDA approval for droxidopa without the substantial evidence of efficacy required to support Northera's approval.

9. First, Defendants decided that they would attempt to invoke the single multicenter study exception (the "multicenter exception") to the Federal Food, Drug, and Cosmetic Act of 1962's (the "**FDCA**"), 21 U.S.C. § 301 *et seq.*, rule that requires two studies. This approach presented two problems: (1) the p-value of Study 301 was more than double the p-value that the FDA had told Chelsea it ***might*** accept for one highly successful study; and (2) more importantly, this exception does not apply to trials like Study 301—where the single multicenter study had a testing center that was disproportionately responsible for the positive results. Out of desperation, Chelsea simply ignored the FDA's prior communications as well as the plain language of the FDCA and embarked on a scheme to defraud the FDA and investors by aggregating the data from Study 301 in its NDA and during its communications with the FDA to conceal from the

FDA and the public that Site 507's results precluded Chelsea from satisfying the multicenter study exception. For example, in December 2010, Defendants began boasting to investors that the Company "intends to accelerate its new drug application" because in a pre-NDA meeting, the FDA changed its previous requirement of two successful studies and "agreed that the proposed NDA for Northera could be submitted based on combined data from Chelsea's two completed Phase III studies in NOH, Study 301 and Study 302, ***without the need for any further efficacy studies***." Press Release, Chelsea, Chelsea Therapeutics Accelerates Northera NDA Filing Following Meeting with FDA (Dec. 20, 2010). The NDA was subsequently completed and filed on September 28, 2011.

10. Eventually, Defendants' scheme began to unravel as the truth was gradually revealed. First, on February 13, 2012, after receiving the FDA staff's Briefing Document for the Cardiovascular Renal Drugs Advisory Committee (CRDAC) (the "**FDA Briefing Document**"), Defendants merely noted that "several lines of inquiry . . . have emerged as significant components of the benefit-risk analysis of Northera" without mentioning the bottom-line, namely, that the FDA staff recommended against Northera's approval. On this news, Chelsea common stock dropped 37.7% on unusually heavy volume.

11. Eight days later, the FDA Briefing Document was published and revealed, *inter alia*, that the FDA recommended against approval of droxidopa because the application lacked evidence showing durability of effect, which was aggravated by several safety concerns, including 18 deaths during the clinical program. The FDA's criticism stood in stark contrast to the misleading description Chelsea had previously provided; thus, on February 22, 2012, the price of Chelsea common stock dropped an additional 28.1%, on unusually heavy volume.

12. Notwithstanding the publication of the FDA Staff Reviewer Dr. Melanie Blank's recommendation, Defendants continued to carry out their fraudulent scheme at the meeting of the Cardiovascular and Renal Drugs Advisory Committee (the "**Advisory Committee Meeting**"), which was held on February 23, 2012 and was open to the public. Specifically, while expounding upon the data demonstrating the safety and efficacy of droxidopa, Defendants failed to ever mention the disproportionate results from Site 507 that rendered Study 301 wholly insufficient under the single multicenter study exception to the FDCA on which Chelsea was relying for approval. Defendants' concealment proved successful in the short term, and based upon the purported efficacy of Study 301 and emotional testimony from patients, a narrow margin of seven of thirteen committee members voted for approval of droxidopa. In response, Chelsea's stock price rose 40%, closing at $3.99 on February 25, 2012.

13. After the Advisory Committee Meeting, the FDA continued its review of the NDA and eventually realized that Defendants had failed to include a breakdown of the data for Study 301 by country and site. When Chelsea ultimately provided the disaggregated data to the FDA, it became clear that Defendants had intentionally concealed the "unusually aberrant" results from Site 507, leaving no doubt that Study 301 did not qualify for the multicenter exception, irrespective of its purported 0.003 p-value, which number was insufficient based on prior FDA communications in any event.

14. On March 28, 2012, Chelsea announced it had received the Complete Response Letter ("**CRL**") from the FDA, which denied its NDA for droxidopa because the application failed to provide sufficient evidence of efficacy and durability of Northera's effect. On this devastating news, the price of Chelsea common stock dropped 28.7% on unusually heavy volume.

15. On May 22, 2012, Chelsea announced that it had met with the FDA to discuss the CRL and disclosed for the first time that droxidopa patients at the highest enrolling site had a disproportionate contribution to the positive results of Study 301. On this news, the price of Chelsea common stock dropped an additional 12% on unusually heavy volume.

16. Defendants' fraud in this case is not unique. The SEC has recently observed that an alarming number of pharmaceutical companies materially misrepresent their communications with the FDA in order to drive up their stock prices. *See* Andrew Ceresney, Director, SEC Division of Enforcement, Remarks at CBI's Pharmaceutical Compliance Congress, 8 (Mar. 3, 2015). Concerned by this growing trend, the SEC warned "that [companies] need to be completely accurate in recounting [their] dealings with the FDA. So much turns on those interactions and not being straight with investors will have significant consequences." *See id.* at 9. Unfortunately this guidance came too late for Chelsea and the Individual Defendants who, during the Class Period, knowingly and/or recklessly made materially false and misleading statements and omitted critical information regarding the development of Northera. Throughout the Class Period, Defendants consistently misled investors regarding the results from Study 301 and the strength of Chelsea's NDA, conditioning investors to believe that droxidopa was likely to be approved by the FDA.

17. Lead Plaintiff hereby brings claims against each of the Defendants named in this action for the losses caused by their respective violations of the federal securities laws.

JURISDICTION AND VENUE

18. This action arises under Sections 10(b) and 20(a) of the Exchange Act, as amended, 15 U.S.C. §§ 78j(b) and 78(t), and SEC Rule 10b-5, 17 C.F.R. § 240.10b-5, promulgated thereunder.

19. This Court has jurisdiction over the action pursuant to 28 U.S.C. § 1331 and Section 27 of the Exchange Act, 15 U.S.C. § 78aa.

20. Venue is proper in this District pursuant to 28 U.S.C. § 1391(b) and Section 27 of the Exchange Act, 15 U.S.C. § 78aa. During the Class Period Chelsea maintained its principal place of business in this District. Certain of the acts and conduct complained of herein, including dissemination of materially false and misleading information to the investing public, occurred in this District.

21. In connection with the acts alleged in this Complaint, Defendants, directly or indirectly, used the means and instrumentalities of interstate commerce, including, but not limited to, the mails, interstate telephone communications, and the facilities of the national securities markets.

PARTIES

22. Plaintiff Roman Zak, as set forth in his shareholder certification and incorporated by reference herein (ECF No. 30-3), purchased Chelsea common stock at artificially inflated prices during the Class Period and has been damaged thereby.

23. During the Class Period, Defendant Chelsea was a Delaware corporation with its principal executive offices located at 3530 Toringdon Way, Suite 200, Charlotte, North Carolina 28277. Chelsea was listed on the NASDAQ under ticker symbol CHTP. On June 23, 2014, Danish pharmaceutical company H. Lundbeck A/S ("**Lundbeck**") acquired Chelsea in a tender offer.

24. Defendant Simon Pedder ("**Pedder**") served as President, Chief Executive Officer ("**CEO**"), and director of Chelsea from April 2004 to July 2012. Because of his positions with the Company, Pedder met with the FDA and had access to the adverse, undisclosed information

concerning the efficacy of droxidopa for patients with NOH, including the disproportionate results from Site 507, the NDA submitted to the FDA, Chelsea's communications with the FDA, and all material facts concerning the development of droxidopa for patients with NOH. Pedder directly participated in and controlled the management of the Company, including, without limitation, the day-to-day decisions concerning the development of droxidopa, submission of the NDA to the FDA, publication of statements made to the investing public, the SEC, and the FDA concerning the efficacy of droxidopa, and publication of statements by and on behalf of Chelsea concerning droxidopa and the NDA in the Company's press releases, SEC filings, and other public statements.

25. Defendant William D. Schwieterman ("**Schwieterman**") has served as Chelsea's Vice President and Chief Medical Officer ("**CMO**") from November 2009 to June 2014. Because of his positions with the Company, Schwieterman met with the FDA and had access to the adverse, undisclosed information concerning the efficacy of droxidopa for patients with NOH, including the disproportionate results from Site 507, the NDA submitted to the FDA, Chelsea's communications with the FDA, and all material facts concerning the development of droxidopa for patients with NOH. Schwieterman also spoke in detail at the Advisory Committee Meeting. Schwieterman directly participated in and controlled the management of the Company, including, without limitation, the day-to-day decisions concerning the development of droxidopa, submission of the NDA to the FDA, publication of statements made to the investing public, the SEC, and the FDA concerning the efficacy of droxidopa, and publication of statements by and on behalf of Chelsea concerning droxidopa and the FDA in the Company's press releases, SEC filings, and other public statements.

26. Defendants Pedder and Schwieterman are referred to herein as the "**Individual**

Defendants."

27. The Individual Defendants, because of their positions with the Company, had the authority to control, correct, and/or update the contents of Chelsea's public disclosures to the market. Each of the Individual Defendants had the duty to exercise due care and diligence and the duty of full and candid disclosure of all material facts relating to the Company's development of droxidopa, communications with the FDA, the efficacy of the drug, and the Phase III trial results. The Individual Defendants further had the duty to correct prior misstatements and/or update any previously issued statements that became materially misleading or untrue, so that the market price of the Company's publicly traded common stock would be based upon truthful, complete and accurate information. To discharge their duties, the Individual Defendants were required to exercise reasonable and prudent supervision over the dissemination of information concerning the Company's development of droxidopa. By virtue of such duties, these officers and directors were required, *inter alia*, to:

a) conduct and supervise the business of Chelsea in accordance with federal laws;

b) supervise the preparation of the Company's SEC filings and approve any reports concerning Chelsea's financial reporting and results; and

c) ensure that Chelsea established and followed adequate internal controls.

28. As officers and/or controlling persons of a publicly-held company which is registered with the SEC under the federal securities laws and the securities of which were traded on the NASDAQ during the Class Period and governed by the provisions of the federal securities laws, the Individual Defendants each had a duty to (i) promptly disseminate accurate and truthful information with respect to the true weaknesses associated with droxidopa's clinical trials and

Chelsea's NDA for the drug; (ii) correct any previously issued statements that were materially misleading or untrue so that the market could accurately price the Company's publicly traded securities based upon truthful, accurate, and complete information; and (iii) update any previously issued statements that became materially misleading or untrue so that the market could accurately price the Company's publicly traded securities based upon truthful, accurate, and complete information.

29. The Individual Defendants are each primarily liable for the false and misleading statements and the scheme to conceal critical data from the FDA and the public alleged herein, and are also liable as controlling persons of Chelsea. The scheme deceived the investing public regarding Chelsea's financial and operational condition and the prospects for obtaining FDA approval for droxidopa in patients with NOH, and caused Plaintiff and other members of the class to purchase Chelsea common stock at artificially inflated prices during the Class Period and suffer damages as a result.

SUBSTANTIVE ALLEGATIONS

A. The FDA Approval Process

30. In the United States, the FDA regulates drugs under the FDCA, 21 U.S.C. § 301 *et seq.* No drug may be marketed in the United States until the drug has received FDA approval. The process required before a drug can be marketed in the United States includes adequate and well-controlled human clinical trials to establish the efficacy of the drug for each indication, submission of the NDA to the FDA, and FDA review and approval of the NDA.

31. Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified clinical investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring

safety, and the effectiveness criteria to be evaluated. Each clinical trial protocol must be submitted to the FDA for clearance. Clinical trials typically are conducted in three sequential phases. The normal clinical trial phases are:

- **Phase I** usually involves the initial introduction of the investigational drug into healthy volunteers to evaluate its short-term safety, dosage tolerance, metabolism pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness.

- **Phase II** usually involves trials in a small patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific indications.

- **Phase III** usually involves further evaluation of clinical safety and efficacy by using the drug in its final form in a larger patient population.

32. The results of clinical trials are often measured by a "p-value" which is the statistical probability of the occurrence of a given finding by chance alone (*i.e.*, a false positive) in comparison with the known distribution of possible findings, considering the kinds of data, the technique of analysis, and the number of observations. A p-value may be noted as a decimal: p <.01 means that the likelihood that the phenomena tested occurred by chance alone is less than 1%. The lower the p-value, the less likely the finding occurred by chance alone. The null hypothesis (*i.e.*, that a treatment has no effect) is rejected when the p-value is less than a pre-determined significance level, which is represented by the symbol α and is ordinarily between 0.05 or 0.01 (5% or 1%). When the null hypothesis is rejected because the p-value is below the significance level α, in which case the treatment may be effective, the result is said to be "statistically significant." In statistics, a Type I error is the rejection of a potentially true null hypothesis, or, in other words, a false positive result. The incidence of false positives is proportional to the number of tests performed and the critical significance level α (*i.e.*, the p-value cutoff); the more hypotheses one tests, the more likely a false positive occurs.

33. Once the required clinical testing is successfully completed, the results of the preclinical and clinical studies, including the relevant p-values, are submitted to the FDA in an NDA. If the FDA approves the NDA, the product can then be marketed for one or more indications. On the other hand, if the FDA reviews the data and deems it to be inadequate to support approval of the NDA, and hence, marketing approval, there is no guarantee that approval will be granted on a timely basis, if at all. The FDA might also refer the NDA to the appropriate FDA advisory committee, typically a panel of clinicians, scientists, industry representatives, and patient advocates, for review, evaluation and a recommendation as to whether the application should be approved.

B. Background of Droxidopa and Neurogenic Orthostatic Hypotension

34. Chelsea sought approval of droxidopa for the treatment of symptomatic NOH in patients with pure autonomic failure primarily associated with Parkinson's Disease ("**PD**"), Multiple System Atrophy ("**MSA**"), and Pure Autonomic Failure ("**PAF**"), as well as Dopamine Beta Hydroxylase Deficiency ("**DβH Deficiency**") and Non-Diabetic Autonomic Neuropathy ("**NDAN**"). *See* Ex. B at 18, Melanie J. Blank, M.D., Clinical Review, FDA (2012).

35. Orthostatic Hypotension ("**OH**") is a reduction of standing systolic blood pressure ("**SBP**") of at least 20 mmHg or diastolic blood pressure of at least 10 mmHg within three minutes of standing. *See id.* at 20. In other words, the person experiences dizziness when standing up. NOH is a subtype of OH and specifically results from the failure of the autonomic nervous system to respond appropriately to changes in posture, resulting in OH on standing. *See id.* at 21.

36. NOH is caused by a decrease in blood pressure upon assuming an upright posture. *See id.* at 20. Typically, patients with NOH lack the ability to auto-regulate their blood pressure

via appropriate vasoconstriction when they rise from a supine to a standing position. *See id.* at 7. Symptomatic NOH is a debilitating condition associated with many symptoms, including dizziness, impaired vision, an inability to think clearly, weakness, fatigue, nausea and balance impairment. *See id.* at 21. Symptomatic NOH can have a profound negative impact on the ability to conduct activities of daily living that involve standing or walking, including the basic activities of personal hygiene and grooming, dressing/undressing and functional transferring (*i.e.*, on/off bed, chair, etc.). *See id.*

37. Global quality of life questionnaires and symptom assessment instruments are not designed to specifically evaluate symptoms of NOH. *See* Horatio Kaufman, et al., *The Orthostatic Hypotension Questionnaire (OHQ): validation of a novel symptom assessment scale*, Clin. Auton. Res. 3 (2011). Therefore, researchers developed the OHQ which has two components: the OHSA to measure the presence and severity of symptoms and the Orthostatic Hypotension Daily Activity Scale ("**OHDAS**") to measure the impact of orthostatic symptoms on daily activities. *See id.* at 4. Part I, OHSA, consists of six questions, each rating the intensity of one characteristic symptom of NOH: (1) dizziness, lightheadedness, feeling faint, or feeling like you might black out; (2) problems with vision (blurring, seeing spots, tunnel vision, etc.); (3) generalized weakness; (4) fatigue; (5) trouble concentrating; and (6) head/neck discomfort. *See id.* Part II, OHDAS, consists of four questions that assess the impact of NOH symptoms on daily activities: (1) activities that require standing for a short time; (2) activities that require standing for a long time; (3) activities that require walking for a short time; and (4) activities that require walking for a long time. *See id.* at 12.

38. There currently are no existing therapies with proven clinical benefit for the treatment of symptomatic NOH. *See* Chelsea Therapeutics International, Ltd., Northera™

(Droxidopa) Advisory Committee Briefing Document 4 (2012) (the "**Chelsea Briefing Document**"). The drug Midodrine is the only medication approved by the FDA for the treatment of symptomatic OH, which was approved using blood pressure as a surrogate outcome measure for symptomatic improvement, but it has not been shown to improve clinical symptoms of NOH. *See id.* Midodrine has significant limitations, including supine hypertension (high blood pressure while lying down) and other adverse events. *See id.* As such, the FDA has determined that there is a significant unmet need for pharmacotherapies that have been proven to provide clinical benefit (*i.e.*, reduction in symptoms and their impact on the ability of patients to perform activities of daily living) and have a favorable side effect profile particularly with respect to exacerbation of supine hypertension. Chelsea aimed to develop droxidopa to fill the void. *See id.*

39. Droxidopa was approved in Japan in 1989 for the treatment of symptoms of frozen gait and OH, syncope, dizziness on standing up and other autonomic disturbances in patients with PD, MSA, and PAF. *See id.* at 129.

40. In 2006, Chelsea obtained development rights from DSP, which had previously marketed the drug in Japan. *See id.* Shortly thereafter, in January 2007, the FDA granted droxidopa orphan drug status for the treatment of symptomatic NOH, which is granted to drugs developed for a disorder affecting fewer than 200,000 people in the United States. *See* Chelsea Therapeutics International, Ltd., Annual Report (Form 10-K), 4 (2009). Orphan drug status also provides seven years of marketing exclusivity and, according to Chelsea "may impact FDA requirements for clinical trials, potentially reducing the time and expense required for such trials." *Id.* The FDA also granted Fast Track designation to droxidopa for symptomatic NOH, which accelerates the review process for products that address serious or potentially life-threatening conditions for which there is an unmet medical need. *See Id.*

41. Three of Chelsea's Phase III trials of Northera are relevant to this action, the details and results of which are briefly displayed in the following chart:

Study	Duration	# of Subjects	Primary Endpoint	Effect	P-Value
301	08/22/08-07/23/10	160	OHQ	-0.9	0.003
302	02/01/08-08/10/09	101	OHSA Item 1	-0.6	0.5
303	04/04/08-10/22/10	75	OHQ	-0.3	0.4

C. Chelsea Worked With The FDA To Develop Its Phase III Trial Program

42. On May 1, 2007, Chelsea met with the FDA to discuss submission of its Investigational New Drug ("**IND**") application for droxidopa. The FDA approved submission of the IND, and during the meeting the "***FDA stated that one study with a [highly significant] p value of ~ 0.00125 might be adequate for approval***." Ex. B at 20. The meeting also "***included a lengthy discussion on the FDA's desire to see durability of effectiveness***[,]" and thus the FDA stressed that "it was important to test the drug over an extended period for the assessment of durability of effect." *Id.* at 80 & 89.

43. Shortly thereafter, on August 21, 2007, Chelsea, including Pedder, then-Vice President of Drug Development L. Arthur Hewitt ("**Hewitt**"), and then-Associate Director of Drug Development Cameron Szakas, met with the FDA for its End-of-Phase 2 Meeting to discuss the size and design of its pivotal Phase III program for droxidopa. *See* Ex. C at 3, Shari L. Targum, M.D., Cross-Discipline Team Leader Review, FDA (2012); Ex. D at 2, End-of-Phase 2 Meeting with Sponsor Minutes (Aug. 21, 2007). At the meeting, Chelsea proposed its plan to conduct Studies 301 and 302 to assess the safety and efficacy of droxidopa in patients suffering from symptomatic NOH associated with PD, PAF, and MSA and Study 303 to supplement Study 302 with additional safety data. The FDA told Chelsea that "***[t]wo phase 3 trials with a clinical endpoint, supplemented with long-term data, would be sufficient for approval***" of droxidopa, if

the studies met their primary endpoints. Ex. A at 3; *see also* Ex. D at 3 ("[T]wo Phase 3 trials involving a clinical endpoint and some long-term data would be sufficient for approval[.]"). The FDA further communicated that the design of Study 303, with three months of treatment and a two week randomized withdrawal period, was acceptable to demonstrate durability of treatment effect. *See id.* at 6.

44. On September 24, 2007, the FDA reviewed and approved the trial protocols for Studies 302 and 303. *See* Ex. C at 3. Chelsea wasted no time and that day announced that it would conduct two pivotal-proof-of-efficacy trials, Studies 301 and 302, "evaluating a combined total of up to 236 patients, thereby reducing the required p-value of each to study to less than 0.05." Press Release, Chelsea, Chelsea Therapeutics Announces Phase III Protocols for Droxidopa Registration Trials to Begin in Fourth Quarter 2007 (Sept. 24, 2007). Pedder also acknowledged the valuable insight the FDA provided regarding what it would take for the Phase III trial program to be successful, stating:

> Our recent meeting with the FDA proved to be a highly productive and collaborative session in which we were able to discuss our options regarding the most effective methods for demonstrating the efficacy, safety and overall therapeutic benefit of Droxidopa in our registration trials for NOH . . . The ongoing dialogue and support from the Agency has proved to be an enormous benefit to the program and we believe our Phase III program is well designed to demonstrate the safety and efficacy required for approval.

45. Following up on the August 21st meeting, on November 28, 2007, the FDA sent Chelsea a letter addressed to Hewitt regarding the proposed terms for Chelsea's Special Protocol Assessment ("**SPA**").[3] *See* Ex. E, Letter from Norman Stockbridge, Director, Division of

[3] The SPA process allows for FDA evaluation of a clinical trial protocol intended to form the primary basis of an efficacy claim in support of an NDA, and provides a binding agreement that the study design, including trial size, clinical endpoints and/or data analyses are acceptable to support regulatory approval. The FDA is not bound by the SPA if, among other things, the sponsor fails to follow the protocol, the relevant data omitted material facts, or a scientific issue

Cardiovascular and Renal Products, to L. Arthur Hewitt, Ph.D., CSO, Chelsea Therapeutics International, Inc. (Nov. 28, 2007). Under Item 1 of the proposed SPA, the FDA clearly stated that ***"[t]he Division expects two successful studies demonstrating efficacy***." Ex. E at 1. Under Item 3, the FDA stated, "to claim sustained long-term effectiveness, the Division recommends that you add a randomized withdrawal phase to the end of the safety study 303. ***Study 301 will give little information about sustained effectiveness***." Ex. E at 2.

46. Study 302 was subsequently initiated on February 1, 2008 (the date on which the first patient enrolled), and enrolled 101 patients in the double-blind phase. *See* Ex. B at 64, 69. Study 302 was a phase III, multicenter, multinational study. *See id.* at 64. The purpose of the study was to compare droxidopa to placebo for the treatment of symptomatic NOH and the primary efficacy endpoint was to test the subject's relative symptomatic change, as measured by the mean score of Item 1 (dizziness or lightheadedness) of the OHSA six-item symptoms assessment scale. *See id.* at 65. Study 302 began with an initial open-label dose titration induction phase (up to 14 days)[4] which was followed by 7 days of open-label treatment, followed by a 14-day randomized withdrawal period and a final clinic visit. There was also a telephone visit 7 days later. *See id.* at 64. Only the subjects who tolerated droxidopa and appeared to have a favorable symptom response during the induction phase were included in the 7-day treatment phase, and only these subjects counted towards the assessment of endpoints. *See* Ex. A at 5. In other words, the deck was stacked with an enriched patient population.

47. In furtherance of Chelsea's plan to conduct two efficacy studies, on February 15,

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essential to determining the safety or efficacy of a drug is identified after testing. *See* Guidance for Industry: Special Protocol Assessment (Food and Drug Admin., 2002).

[4] During the dose titration, induction phase of a trial, the investigator begins treatment with an initial low-dose of the drug and then carefully adjusts the dose upward until the patient experiences a response. Titration allows the body to adjust to the drug and avoid harmful side effects.

2008, Chelsea met with the FDA to further discuss the terms of the SPA for Study 301. *See* Ex. B at 20. During this meeting, the FDA stated clearly that it "***expected two successful trials***" with a p-value of less than 0.05 to support efficacy. Ex. A at 3; Ex. B at 20.

48. Study 301 was initiated on August 22, 2008 (the date on which the first patient enrolled) and subsequently enrolled 162 subjects in its double-blind phase. *See* Ex. B at 8, 32. Study 301 was a phase III, multicenter, multinational study with an initial open-label dose titration induction phase (up to 14 days), followed by a 7-day washout period, followed by a 7-day double-blind randomized treatment period with at least 75 patients randomized to placebo and at least 75 patients randomized to droxidopa. *See id.* at 32. Similar to Study 302, only those subjects who tolerated droxidopa and appeared to have favorable symptom response during the 1-2 week titration phase were permitted to undergo treatment. *See id.* at 34. As well, only those responder subjects counted toward the assessment of endpoints. Ex. A at 5. The study was designed to evaluate the clinical effect (efficacy and safety) of droxidopa treatment (versus placebo) in patients with symptomatic NOH and PD, MSA, PAF, DβH Deficiency, or NDAN. *See* Ex. B at 32. The original primary endpoint for Study 301 was OSHA Item 1.[5] *See id.* at 36.

49. On September 24, 2009, Chelsea announced top-line results from its first completed study, Study 302. *See* Press Release, Chelsea Therapeutics Reports Preliminary Phase III Data of Droxidopa for Treatment of Symptomatic Neurogenic Orthostatic Hypotension (Sept. 24, 2009). The results indicated that the study failed to meet it primary efficacy endpoint, improvement in OHSA Item 1, and also failed to show a difference in standing SBP between placebo and droxidopa. *See id.* at 1. Chelsea's after-the-fact exploratory analysis did show a

[5] As a result of Study 302's failure to meet its primary endpoint, Chelsea changed the primary efficacy endpoint mid-study from the OHSA Item 1 score to the entire OHQ score as set forth in ¶50.

nominally statistically significant improvement in the OHQ composite score. *See* Press Release, Additional Analysis Confirms Significant Symptomatic Benefit of Droxidopa in Treatment of Neurogenic Orthostatic Hypotension (Oct. 1, 2009). Since Study 302 utilized a randomized withdrawal design, Chelsea expected the placebo group would worsen, because the patients had been taken off the drug, and the droxidopa group to stay the same, or ideally, even improve. Both groups, however, worsened considerably. *See* Sept. 24, 2009 Press Release. Not only did these results "clearly . . . draw the efficacy of droxidopa into question," Ex. B at 70, but they also revealed fundamental doubts about Northera's future.

50. As a result of these troubling findings, half-way through Study 301, Chelsea was forced to reach out to the FDA to discuss altering Study 301's primary efficacy endpoint, which was the same endpoint as failed Study 302. *See* Ex. B at 36. Additionally, in conjunction with Chelsea's request for a change in Study 301's primary endpoint, the Company requested feedback from the agency regarding the size and powering of Study 301, as well as the suitability of filing an NDA based on Study 301 and failed Study 302. *See* Press Release, Chelsea Therapeutics Granted Approval to Change the Primary Endpoint and Increase Enrollment in Droxidopa Pivotal Study 301 (Dec. 15, 2009) (the "Dec. 15, 2009 Press Release"). On November 18, 2009, Chelsea and the FDA met to discuss Chelsea's proposal. *See* Ex. C at 4. The FDA stated that it "does not believe that a secondary or subgroup analysis of 302 contributes to ***the two successful studies needed for approval***. Study 302 could not be used as a pivotal study since it failed to meet its primary outcome measure." *Id.* Therefore, the FDA "recommended that Chelsea submit a confirmatory study to support an NDA filing" and indicated that such a study should be contained to a small, highly enriched, homogenous patient population. *See* Dec. 15, 2009 Press Release. Chelsea announced on December 15, 2009 that

the FDA had allowed the Company to change the primary endpoint for Study 301, and more significantly, that Chelsea would initiate a new clinical trial, Study 306, early in 2010, as a confirmatory study for its NDA. *See id.*

51. The Company later announced on February 25, 2010 that Study 306 would be a multinational Phase III trial evaluating up to 84 patients with symptomatic NOH associated with PD. *See* Press Release, Chelsea Therapeutics International, Ltd. Recent Developments (Feb. 25, 2010). The trial would be approximately twelve weeks in duration and include an initial, blinded dose titration period lasting up to two weeks, after which all patients would continue on to an eight-week double-blind treatment period. *See id.* As in Study 301, the primary endpoint of the trial would be the relative improvement in the OHQ composite score between droxidopa and placebo. *See id.* The Company also anticipated that data from this trial would be ready in the second quarter of 2011, allowing for Study 306 to be included in an NDA filing later in 2011. *See id.*

52. Study 301 was ultimately completed on July 23, 2010 and met its amended endpoint, distinguishing itself as the only successful study supporting the NDA. *See* Ex. B at 32. The results showed a statistically significant improvement in the OHQ composite score, with a p-value of 0.003. *See* Ex. A at 9. These positive efficacy results, however, were severely undermined by the disproportionate contribution from one of the testing sites. That is, of the thirteen testing sites used in Study 301—Site 507, State Medical Academy in Dnipropetrovsk, Ukraine—enrolled 16 subjects, or 10% of the trial, but was responsible for 37% of the overall effect on the endpoint. Site 507 also treated 6 of the 14 patients (43%) who showed improvement in their OHQ composite score by more than 4 units—the so-called "super responders." *See* Ex. A at 13. As demonstrated in the chart below, the p-value of 0.000000005

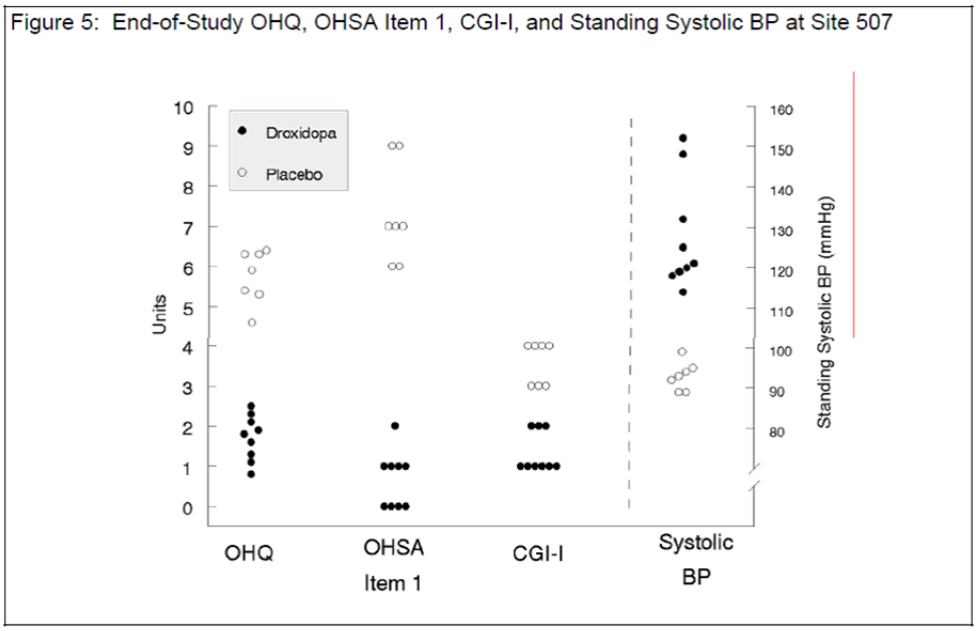
from Site 507 was conspicuously smaller than that of any other testing site:

Table 2: OHQ Results by Study Site

Site Number - Name	Country	N	Delta (units)	P-value
507 - State Medical Academy	Ukraine	16	-3.6	0.000000005
505 - Central Clinical Hospital Ukrzaliznytsia	Ukraine	11	-1.7	0.007
100 - Arkansas Cardiology	US	6	-1.3	0.77
103 - Mayo Clinic - Arizona	US	6	-1.2	0.55
300 - Universita di Bologna	Italy	5	-1.1	0.63
125 - The Movement Disorder Clinic of Oklahoma	US	9	-1.0	0.50
512 - Kyiv City Clinical Hospital No 3	Ukraine	5	-0.8	0.10
607 - Private Neurology Practice: Radomir Talab	Czech Rep	8	-0.3	0.77
105 - Baylor College of Medicine	US	5	-0.1	0.39
501 - Insitute of Neurology Psychiatry and Narcology	Ukraine	6	0.5	0.73
706 - Dr Falup - Pecurariu Cristian	Romania	5	0.5	0.68
601 - Med Point sro	Czech Rep	4	1.1	0.50
126 - Neurosearch II Inc	US	5	2.2	0.27

Id. When the study's overall p-value is calculated without Site 507, it increases from 0.003 to 0.07, which, as the FDA noted, is no longer statistically significant. *See id.* at 13-14.

53. Also suspicious, the data showed that the within-group variances "for all of the important end-of-study measures (composite OHQ, Item 1 of the OHSA, the CGI-I score, and standing systolic BP[)]" were exceedingly small. Ex. A at 13-14; Ex. F at 5, Letter from John Jenkins, Director, Office of New Drugs, Center for Drug Evaluation and Research to Joseph Oliveto, Interim President and CEO, Chelsea Therapeutics International, Inc. (Feb. 8, 2013). "That is, patients in the droxidopa group showed consistently large improvement in all three outcomes, whereas patients in the placebo group showed consistently negligible improvement or worsening" (Ex. F at 5):



Ex. A at 13-14; Ex. G at 5, Memorandum of Meeting Minutes, May 2, 2012. As well, despite the rarity of PAF, Site 507 enrolled numerous patients within a span of only a few days. *See* Ex. G at 7.

54. The data from Site 507, which Dr. Unger described as "truly extraordinary," was of great concern to Chelsea; and, as a result, the Company audited the site on two occasions, including at least once during the course of the trial, but the Company was purportedly unable to find any evidence of wrongdoing. *See* Ex. F at 6. Regardless of whether the results were fraudulent, it was clear to Defendants that Site 507 was disproportionately responsible for the positive effect seen in Study 301.

55. Study 303 was the third efficacy and safety study conducted by Chelsea during the Class Period. Study 303 began on April 4, 2008 and was a three-month extension study that was designed to provide long-term drug treatment for patients with symptomatic NOH who previously demonstrated a symptomatic benefit from droxidopa treatment in Study 301 or failed Study 302. *See* Chelsea Briefing Document at 58. After three months, the patients were also

randomized on a 1:1 basis to either continue their Northera treatment or be withdrawn to placebo for a blinded two-week period to assess the comparative safety and durability of effect of Northera against placebo. *See* Ex. B at 80. The primary efficacy endpoint of the two-week period was a statistically significant reduction in the OHQ composite score. *See id.* at 79. At the end of the two-week period, Study 303 failed to meets its primary efficacy endpoint because ***the OHQ composite score rose 0.90***. *See id.* at 82.

D. Chelsea's Fraudulent Scheme To Hide The Material Weaknesses In Its Study Data And NDA From The FDA And Investors

56. In light of the failures and weaknesses in the study results for Northera, as well as the doubts as to Chelsea's ability to continue as a going concern, *see* ¶166 below, Defendants devised a fraudulent scheme in an effort to save Chelsea and its Northera development program. Well aware of the FDA's recommendation that Chelsea submit two successful efficacy studies and evidence of Northera's durability of effect, Defendants realized that they did not have such data in light of Study 302's failure. In an effort to save the development program and the Company, Defendants decided that they would press forward with the NDA based on Study 301's questionable results by attempting to invoke the FDCA's multicenter exception. Significantly, however, in order for the scheme to have any chance of success, Defendants would have to—and in fact did—conceal the disproportionate results from Study 301's Site 507 from the FDA because, as explained below in ¶¶69-70, this exception would not apply in situations like Chelsea's where a single site in a multicenter study was disproportionately responsible for the favorable effect seen.

57. On December 1, 2010, Chelsea, including Chief Scientific Officer Hewitt, Schwieterman, Szakas, Senior Director of Preclinical Programs, Gerry Rowse, and Vice President of Operations, Joseph Oliveto, met with the FDA in a pre-NDA meeting to discuss

Chelsea's proposed submission of an NDA based on the results of Study 301 under the multicenter exception. *See* Ex. C at 4; Ex. H at 2, Memorandum of Meeting Minutes, Dec. 1, 2010. During the meeting the FDA stated that Study 306 could be omitted from the clinical section of the NDA and instead provided as supplementary information upon study completion. *See* Ex. C at 4. More significantly, during the meeting, the FDA reminded Chelsea that although it could submit an NDA based on the multicenter exception:

> ***it is not customary for the Agency to approve a new chemical entity with only one positive efficacy trial.*** Furthermore, because you have reported cases of angina, heart failure, and arrhythmias in your small development program, it is possible that a complete review of your safety data will suggest that the current exposure in your development program is inadequate or that the safety profile is incompatible with your established benefits.

Ex. H at 3; *see also* Ex. A at 4 ("the FDA reminded Chelsea that one trial is not usually sufficient for approval."). At no point during the meeting or its prior communications with the FDA did Chelsea disclose Site 507's disproportionate effect on Study 301's results.

58. As a result of this meeting, on December 20, 2010, Chelsea announced that it "intend[ed] to ***accelerate*** its new drug application" for droxidopa. Press Release, Chelsea, Chelsea Therapeutics Accelerates Northera NDA Filing Following Meeting with FDA (Dec. 20, 2010). Rather than disclose the FDA's reminder that it expected to see two studies showing efficacy or that without Site 507, Study 301's results would not have been statistically significant, and notwithstanding the FDA's prior communications, Chelsea instead boasted, "the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from Chelsea's two completed Phase III studies in NOH, Study 301 and Study 302, without the need for any further efficacy studies." *Id.*

59. Tellingly, securities analysts following the Company interpreted Chelsea's announcement that the FDA was willing to consider Chelsea's droxidopa NDA based solely on

Study 301 and failed Study 302 as a positive step towards FDA approval. For example, in a January 26, 2011 Ladenburg Thalmann Report, analyst Juan Sanchez stated that "the December 20, 2010 announcement . . . in our view, ***significantly reduced the regulatory risk*** for Northera and increased the value of CHTP (for this reason, we increased our [Price Target] to $10.50 from $8.00 on December 21, 2010)." Likewise, Chelsea's stock price rose $1.68, or approximately 28%, on December 20, 2010.

60. Shortly thereafter, on February 2, 2011, the Company announced plans to modify Study 306 following a futility determination at the planned interim analysis of the study's primary endpoint. *See* Press Release, Chelsea Therapeutics Announces Interim Results to Modify Study 306 to Focus on Reduction in Falls Associated With Neurogenic Orthostatic Hypotension (Feb. 2, 2011). At the end of the eight-week double-blind treatment period, patients taking droxidopa reported a mean improvement in OHQ composite score of 2.3 units from their mean baseline OHQ composite score of 6.0, established prior to drug treatment. *See id.* The study's ability to discern the true benefit of droxidopa was confounded by a highly variable placebo response, resulting in a relative mean difference of 0.2 units in OHQ composite scores between droxidopa and placebo at the end of the study. *See id.* As a result of the futility determination, Chelsea yet again endeavored to shift the primary endpoint of its study to focus on the prevention of falls in PD patients. *See id.*

61. Having already enrolled 113 patients, Chelsea announced plans to modify and separate Study 306 such that the first 51 patients evaluated in this unblinded analysis would be considered Part A (306A) and constitute a hypothesis-generating study, and the remaining patients enrolled in the study would become Part B (306B) and serve as a distinct, hypothesis-confirming study. *See id.* At the time, Chelsea anticipated data from 306B to be available by the

second quarter of 2012. *See id.*

62. On September 28, 2011, after confirmatory Study 306 failed, Chelsea announced that it submitted an NDA to the FDA for approval to market Northera for treatment of symptomatic NOH. Notably, Chelsea's NDA did not note or discuss the fact that Study 301 would not have been statistically significant without Site 507 or that Site 507 in Ukraine was disproportionately responsible for the study's results. On November 17, 2011, the FDA accepted Chelsea's filing for review, also granting Priority Review, which the FDA grants to drugs which potentially offer major advances in treatment or provide a treatment where no adequate therapy exists. The Company indicated that the FDA would review and act on the NDA by March 28, 2012.

63. The NDA Chelsea submitted to the FDA for approval of droxidopa contained material known weaknesses. Specifically, Studies 302 and 303 failed to achieve their primary endpoints, and the only study potentially demonstrating any clinical efficacy, Study 301, suffered from disproportionate results from Site 507. Finally, as set forth above, during the Class Period the FDA "provided clear and consistent advice that ***2 studies showing effectiveness***, each with a p-value <0.05, ***were expected***, that a single study could be adequate ***if the p-value was approximately 0.00125***, and that ***providing evidence of durability of effect***, as study 303 was intended to provide, ***would be important***." Ex. A at 4. Yet, the NDA relied solely on the efficacy of Study 301, which had a p-value of 0.003—again, only due to the results of Site 507—and failed to demonstrate any durable effect (*i.e.*, at least three months).

64. As an initial matter, the FDA requires longer-term data for chronic disease treatments, because "patients should not be exposed to a drug chronically unless benefit is established over a reasonable amount of time – at least three months." *See* Ex. B at 17. As noted

by Dr. Unger in the Office Director Decisional Memo, "NOH represents a set of chronic diseases, and the [FDA] had been quite clear with its recommendation to the applicant to provide a demonstration of the durability of droxidopa's effect." Ex. A at 18.

65. Also, the FDCA requires manufacturers of drug products to establish a drug's effectiveness by "substantial evidence." Substantial evidence is defined as:

> [E]vidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended or suggested in the labeling or proposed labeling thereof.

FDCA § 505(d), 21 U.S.C. § 355(d).

66. According to the FDCA, the FDA requires at least two adequate and well-controlled studies, each convincing on its own, to establish effectiveness. FDCA § 505(d). There are, however, three scenarios where it might be acceptable to consider less than two successful efficacy trials for approval. *See* Ex. I at 6, Guidance for Industry: Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products (Food and Drug Admin., 1998).

67. The first scenario occurs where effectiveness of a new use for a drug may be extrapolated entirely from existing positive efficacy studies. *See id.* at 10. This condition generally applies to drugs that are already approved and are seeking another indication, another population, or another dosage form. *See id.*

68. In the second scenario, a single study of a new use can demonstrate effectiveness with independent substantiation from related study data. *See id.* at 11. In other words, a single adequate and well-controlled study of a specific new use can be supported by information from other related adequate and well-controlled studies, such as studies in other phases of a disease, in

closely related diseases, of other conditions of use (different dose, duration of use, regimen) of different dosage forms, or of different endpoints. *See id.*

69. The third scenario, the multicenter exception, addresses situations in which a multicenter study, without supporting information from other adequate and well-controlled studies, may provide evidence that a particular drug is effective. *See id.* at 15. The FDA has explicitly stated that it will consider this scenario "only when results are strong." Statement Regarding the Demonstrations of Effectiveness of Human Drug Produces and Devices, 60 Fed. Reg. 39,181 (Aug. 1, 1995). A conclusion based on two persuasive studies will always be more secure than a conclusion based on a single, comparably persuasive study. *See* Ex. I at 16. For this reason, reliance on only a single positive study will generally be limited to situations in which a trial has demonstrated a clinically meaningful effect on mortality, irreversible morbidity, or prevention of a disease with potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible. *See id.* The following characteristics demonstrate instances when a single adequate and well-controlled multicenter study that, although not determinative, ***might*** support an effectiveness claim:

- In a large, multicenter study in which no single study site provided an unusually large fraction of the patients, and ***no single investigator or site was disproportionately responsible for the favorable effect seen***, the study's internal consistency lessens concerns about lack of generalizability of the finding or an inexplicable result attributable only to the practice of a single investigator. ***If analysis shows that a single site is largely responsible for the effect, the credibility of a multicenter study is diminished***.
- Consistency across study subsets.
- Multiple studies in a single study.
- Multiple endpoints involving different events.
- Statistically persuasive findings.

See id. at 16-18.

70. The FDA guidelines note that, while the FDA may acknowledge the persuasiveness of a single, internally consistent, strong multicenter study, even a strong result can represent an isolated or biased result, ***especially if that study is the only study suggesting efficacy among similar studies***. ***When considering whether to rely on a single multicenter trial, the FDA must consider the possibility of an incorrect outcome*** and that all available data is examined for its potential to either support or undercut reliance on a single multicenter trial. *See id.* at 18.

71. Further, when an NDA does rely upon a single multicenter trial, FDA guidance requires that the application present "individual center results" separately and "[a]ny extreme or opposite results among centers should be noted and discussed." Ex. J at 74, Guideline for the Format and Content of the Clinical and Statistical Sections of an Application (Food and Drug Admin., 1988) ("**Format Guidance**") ("Key efficacy measures should be displayed by investigator and the larger studies should be analyzed separately.").

72. Despite knowing full well that the droxidopa development program did not comply with the FDA guidelines and recommendations described above, Defendants continued to mislead investors regarding their communications with the FDA, the results from Study 301, and the strength of Chelsea's NDA, conditioning investors to believe that droxidopa was primed to be approved by the FDA.

E. Advisory Committee Meeting—The NDA's Flaws Are Partially Exposed

73. On January 3, 2012, Chelsea announced that the FDA scheduled a meeting of the Advisory Committee for February 23, 2012 to review droxidopa's NDA and provide non-binding guidance regarding approval. Prior to the meeting, on February 1, 2012, Chelsea,

including Pedder, Schwieterman, Hewitt, Oliveto, and Rowse, attended a conference call with the FDA to "discuss any pending issues[.]" Ex. K at 2, Memorandum of Teleconference Minutes, Feb. 1, 2012. During the call, Dr. Stockbridge expressed concern that "the sponsor had ***insufficient long-term data to address the question of durability of effect*** . . ." *See id.* at 3-4.

74. On February 13, 2012, Chelsea announced that the FDA had provided the Company with the FDA Briefing Document, which the FDA staff had prepared for, *inter alia*, the Advisory Committee Meeting. *See* Press Release, Chelsea Therapeutics CEO to Review NORTHERA NDA and Provide an Update on Upcoming Advisory Committee Meeting During Presentation at BIO CEO (Feb. 13, 2012) (the "Feb. 13, 2012 Press Release"). The FDA Briefing Document concluded against approval of droxidopa "***[o]n the basis of the safety concerns compounded by absence of evidence of durability of effect***." *See* FDA Briefing Document at 13. However, in Chelsea's press release, the Company omitted the FDA Briefing Document's ominous conclusion, simply stating that "several lines of inquiry . . . have emerged as significant components of the benefit-risk analysis of Northera," and provided a summary of issues that had been "previously discussed." *See* Feb. 13, 2012 Press Release. Defendant Pedder disclosed, in part:

> A number of these questions [in the FDA Briefing Document] ***relate to previously discussed issues identified for our development program, namely the short duration of our clinical studies***, the limited size of our study population given the orphan indication and the challenges in quantifying symptomatic and clinical benefit. FDA has, however, placed increased emphasis on safety data from our long-term extension program and the post-marketing surveillance program in Japan. We look forward to the opportunity to address these questions in depth during the advisory committee meeting and to continuing to work with FDA to address any additional questions they may have regarding Northera and our clinical program.

75. On this news, the price of Chelsea common stock dropped $1.88 per share, or 37.7%, to close at $3.11 per share on February 14, 2012 on unusually heavy volume.

76. On February 21, 2012, the FDA publicly released on its website the FDA Briefing Document, which reiterated what the FDA had previously told the Company the FDA expected two efficacy studies and at least one study showing durability of effect. Specifically, the FDA Briefing Document stated that on May 21, 2007 the FDA told the Company "that one study with a p value of ~ 0.00125 might be adequate for approval" and "on December 10, 2010, the FDA reminded Chelsea that one trial is not usually sufficient for approval." *See* FDA Briefing Document at 16. The FDA Briefing Document also highlighted the fact that ***"[c]linical study 301 is the only study in this NDA that won on its primary endpoint***." *See id* at 28.

77. The strong, critical language of the FDA Briefing Document stood in sharp contrast to Chelsea's February 13, 2012 characterization of the FDA's staff position. In support of its recommendation against approval, the FDA Briefing Document cited the studies' failure to demonstrate durability of effect of droxidopa in light of "the worrisome safety signals that arose during the open-label phases of the trials which included deaths, strokes, myocardial infarction, progression of underlying disease, and hypertensive crisis" and the Japanese postmarketing cases of neuroleptic malignant syndrome, which can be fatal. *Id.* Specifically, the FDA cited the following reasons for its recommendation against approval:

> ***There has been no durable effect (i.e., more than 4 weeks) demonstrated for droxidopa and the safety profile is not clear because of the design of the trials.*** Studies 302 and 303, while showing the slightest of favorable trends on OHSA Item 1 (0.6 effect size, p=0.51 for Study 302 and 0.4 effect size, p = 0.25 for Study 303), ***did not demonstrate*** clinical/symptomatic benefit for droxidopa after two weeks and 3 months, respectively, of chronic use followed by a 2-week randomized withdrawal period. These studies also failed to show any durable effect on systolic blood pressure. . . .
>
> ***It is important to consider failure to demonstrate durability of effect in light of generally insufficient safety data*** and concerning safety findings including 18 deaths in the open-label phase, 2 strokes on post-mortem examination and 1 other stroke in a patient who survived, 2 AEs of hypertensive crisis, 1 myocardial infarction (resulted in death), 1 case of coronary artery disease that resulted in

> discontinuation, 33 cases of worsening of underlying movement disorder including 2 SAEs, in addition to many other SAEs and discontinuations. Additionally, in the Japanese postmarketing experience, there were 9 reported cases of neuroleptic malignant syndrome, an often fatal condition. A few of these cases appeared to have no likely etiology for what is considered to be a serious iatrogenic condition. The data that the sponsor provided was insufficient to conclude or exclude causal relationships. It is difficult and imprudent to assign causalty to droxidopa because of the mostly open-label design of the study and the nature of postmarketing reporting periods. Nevertheless, the specter of serious safety issues related to droxidopa has been raised and should not be ignored. . . .
>
> ***In the FDA guidance titled, "Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products", the following is also written: "When considering whether to rely on a single multicenter trial, it is critical that the possibility of an incorrect outcome be considered and that all the available data be examined for their potential to either support or undercut reliance on a single multicenter trial." Certainly, approval of droxidopa with no postmarketing commitment would leave many safety and durability of efficacy questions unanswered.***

Id. at 11-12.

78. On this news, the price of Chelsea common stock dropped $0.94 per share, or 28.1%, to close at $2.41 per share on February 22, 2012 on unusually heavy volume. Tellingly, that day Bloomberg.com led with the headline that Defendants omitted in their press release eight days earlier: "Chelsea Therapeutics Northera Shouldn't Be Approved on Safety, FDA Says." *See* Anna Edley, *Chelsea Therapeutics Northera Shouldn't Be Approved on Safety*, FDA Says, Bloomberg.com (Feb. 21, 2012, 4:08 PM), http://www.bloomberg.com/news/2012-02-21/chelsea-therapeutics-northera-shouldn-t-be-approved-on-safety-fda-says.html.

79. At the Advisory Committee Meeting, the panel raised efficacy and durability concerns. The committee agreed that Studies 302 and 303 were failures that "do not provide confirmatory evidence of benefit." Ex. L at 321, Transcript of Cardiovascular and Renal Drugs Advisory Committee Meeting (Feb. 23, 2012). Even Study 301 "did not provide evidence regarding the duration of effect in any direct way." *Id.* In fact, as underscored by the discussion

between Advisory Committee Meeting participants Dr. Steve Grant[6] and Dr. Temple, the results were disappointing on both fronts:

> **Dr. Steve [Grant]:** ***The very first thing we said in the SPA is that the study in and of itself wouldn't be sufficient, that we wanted two studies. We also said that we wanted durability***, that we expect this is a chronic disease and we expected long-term data. ***That was repeated on at least two subsequent occasions on information letters to the company***. So I just wanted to clarify that the review that was done here is not significantly different from what they were told.
>
> **Dr. Temple:** Steve, ***doesn't it say we expect two studies?*** . . . That's not quite the same thing as what you said.
>
> **Dr. [Grant]:** Well, yes, but we said we expect two studies. The question was, you didn't answer was, was two studies mentioned in the SPA; was there an agreement—the question was . . . was this study in and of itself going to be sufficient, if successful, to support an application? And we never know what the answer is. As Norman says, an overwhelming effect in one study, you'd be a fool not to approve it.
>
> **Dr. Temple:** That's the point I'm making, Steve. We said we expect two studies. That's true. We do. It didn't say, there's no possibility that only one study will—
>
> **Dr. [Grant]:** That's correct. But that wasn't the question.

Id. at 282-284.

80. In regard to efficacy, Dr. Sanjay Kaul, an Advisory Committee panelist, went so far as to accuse Chelsea of changing the statistical methodology after seeing the raw unblinded data from the clinical trials:

> [Chelsea claims] that there is confirmatory evidence of benefit derived from Study 302. And I would say, no; ***you are peeking at the data, and then you are cherry-picking the endpoint to—you know, you're going on a fishing expedition, essentially, to find a statistically significant difference***. And you find that, and then you redesign your other study [301]. Then you can claim the study as your confirmatory evidence of the treatment effect. It is hypothesis-generating.

[6] Plaintiff believes the doctor referred to as Dr. Steve Graham in the transcript is actually named Dr. Steve Grant.

Id. at 315.

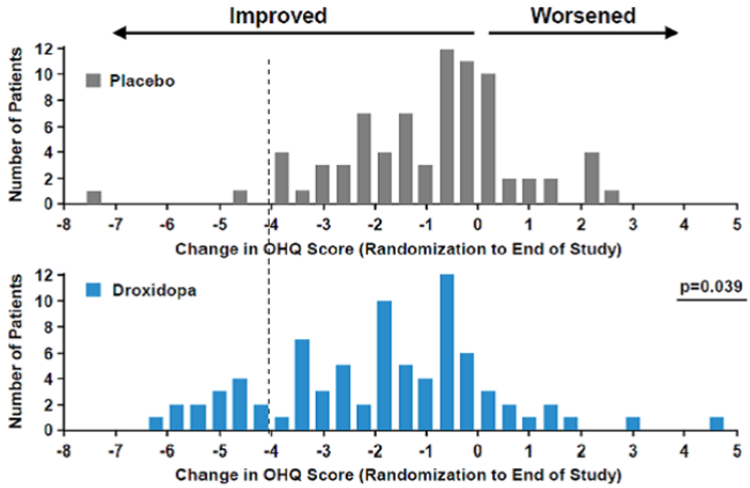
81. In regard to durability of effect, according to Dr. Philip Sager, a panelist on the Advisory Committee, the Chelsea trials provided "no evidence, really at all, of any effects that are really greater than a week in length life in a randomized, controlled cohort." *Id.* at 297. Dr. Mori Krantz, another panelist on the Advisory Committee, described the Chelsea trials as "the shortest study ever in the history that I've ever seen, reading the scientific literature." *Id.* at 326. A third Advisory Committee panel expert, Dr. Scott Emerson, added that "there [are] too many unanswered questions here that make this short time period just completely inadequate." *Id.* at 328. While failed Study 303 had a treatment period of three months, according to the Advisory Committee, the results were virtually meaningless as the study provided no statistically significant "evidence of benefit" nor did it provide evidence to support duration of effect. *Id.* at 321.

82. The Chairperson of the Advisory Committee, Dr. A. Michael Lincoff, best summarized the panel's concerns regarding the droxidopa trials, stating "virtually all [members of the Advisory Committee] agree that the other studies do not provide confirmatory evidence of benefit. And the primary study, the 301[,] also did not provide evidence regarding the duration of effect in any direct way . . . ." *Id.* at 321.

83. Despite these concerns, the Advisory Committee recommended droxidopa for approval with a vote of seven to four with one abstention and one non-vote. *See id.* at 379. The seven of thirteen members of the Advisory Committee—which included industry and patient representatives—who voted to approve droxidopa found that droxidopa afforded at least some patients with a clinically meaningful symptom benefit based upon the emotional anecdotal testimony of droxidopa patients who attended the meeting. *See id.* at 300, 334. According to Dr.

Unger, upon examining the following histogram showing that fourteen subjects in the droxidopa group, versus two in the placebo group, improved by at least four points on the OHQ, "some members of the Advisory Committee seemed convinced that droxidopa afforded at least some patients a clinically meaningful symptom benefit":

Figure 4: Study 301: Histogram of Responses for the OHQ Score, the Primary Study Endpoint (Applicant's Slide CR-70; 2/23/12 Advisory Committee Meeting)



Ex. A at 11-12. As Dr. Jenkins later explained: "These 'super responders' were of great interest to members of the AC who voted in favor of approval[.]" Ex. F at 5.

84. Dr. Papademetriou justified his vote in favor of approval as follows:

> I think this is a devastating disease, and for those who have it, this makes their life unbearable. And we don't have an effective therapy for these patients at this time. So I'm making available a drug that can help, admittedly, not all of them, but some of them. . . . And I could not in a clear conscience vote no and deprive those patients from the benefits they can derive at this point from this medication. Sure, I feel the need to collect more data and see more studies, and the postmarketing surveillance data would be helpful, although they are not optimal.

Ex. L at 386-387.

85. Although the vote was not binding on the FDA, on the conference call held immediately after the Advisory Committee Meeting, Chelsea expressed extreme confidence in its application. Dr. William White, a cardiologist who spoke at the meeting on Chelsea's behalf,

even went so far as to trash the doctor who drafted the FDA Briefing Document, stating "based on the way [the FDA Briefing Document] was written and based on the presentation today by that medical officer" he concluded "that she was very naïve and this was probably one of the first times she's ever done this." Dr. White's statements were not only impolite, they were incorrect: Dr. Blank has worked as medical reviewer for the FDA for more than ten years.

86. Excited by this news, investors drove up the price of Chelsea stock by 40%, causing it to close at $3.99 on February 25, 2012.

87. Unbeknownst to investors, however, was that the Advisory Committee's decision was made without knowledge of the disproportionate results from Site 507 set forth in ¶¶52-54 above, namely that the p-value from Site 507 was solely responsible for the statistically significant result and that six of the fourteen subjects who experienced an improvement of four or more points—the so-called "super responders"—were tested at Site 507. Indeed, in contravention of the FDA's Format Guidance, Chelsea chose to aggregate Study 301's results in the NDA and did ***NOT*** provide a break-down of the data by testing site or country. *See* Ex. A at 12. It was not until "[l]ate in the review cycle, after most of the reviews were filed" and after the Advisory Committee Meeting had been held that "the review team recognized that the applicant had not provided the 301 study results by center or by country." Ex. A at 12; Ex. G at 7.

88. When Chelsea finally provided the disaggregated results of Study 301 to the FDA, the FDA was shocked by the "unusually aberrant, and quite remarkable" data from Site 507 and found its results "too good to be true." Ex. A at 15; Ex. G at 7.

F. The FDA Rejects Chelsea's NDA

89. The disproportionate results from Site 507 put the final nail in the NDA's coffin, and the FDA determined that further testing would be required for approval. *See* Ex. A at 17.

Thus, on March 28, 2012, Chelsea received the CRL from the FDA denying approval of droxidopa. *See* Ex. M, Complete Response Letter from FDA to Chelsea (Mar. 28, 2012). The CRL explained that the NDA was not sufficiently supported by evidence of efficacy and durability of effect.

90. In regard to efficacy, the CRL provided the following reasoning:

- When considering whether to rely on a single adequate and well-controlled trial, our Guidance tells us to consider critically the possibility of a false positive result, in part by examining all the available data. Here the results of studies 302 and 303 undercut the persuasiveness of study 301. Despite the enrichment strategy used in studies 302 and 303 to select subjects who both respond to and tolerate the drug, neither study succeeded on its primary endpoint. ***Inconsistencies in the overall findings, therefor, constitute a reasonable basis for not accepting study 301 alone as adequate evidence of effectiveness***.

- Our Guidance also explains that for a single study to support effectiveness, ***"(1) no single study site . . . (should provide) . . . an unusually large fraction of the patients and (2) no single investigator or site . . . (should be) . . . disproportionately responsible for the favorable effect seen . . . If the analysis shows that a single site is largely responsible for the effect, the credibility of a multicenter study is diminished." In examining the results of study 301, Site 507 was disproportionately responsible for the overall treatment effect: Site 507 contributed only 10% of the subjects, but the results there were strikingly positive and provided much of the overall effect size. Specifically, the p-value for the primary efficacy endpoint of the study as a whole was persuasive (0.003), yet the results are no longer statistically significant when subjects from Site 507 are removed from the analysis. The disproportionate contribution of Site 507 to the overall results of study 301 diminishes the persuasiveness of the study, providing even stronger reason for not accepting study 301, the sole positive study, as adequate evidence of effectiveness***.

Ex. M at 2.

91. In regard to durability of effect, the CRL provided the following reasoning:

- ***During development, the Division stressed the importance of providing evidence for the durability of droxidopa's effect***; however, the study with the best potential to show this, study 303 . . . did not succeed. Similarly, study 302 . . . did not support durability of treatment effect. Thus, none of the submitted studies show durability of effect beyond one week.

- ***Prior to submission of the NDA, we advised you that it would be important to provide evidence of durability of droxidopa's treatment effect.*** The advice has not changed, and the issue has not been addressed adequately in your development program.

Ex. M at 1-2.

92. The FDA's Office Director Decisional Memo, drafted by Director Dr. Unger and dated March 28, 2012, provided the FDA's reasoning for denying approval of droxidopa. *See* Ex. A. The memo began with a review of the FDA's expectations for the NDA stating, "[t]he Division provided clear and consistent advice that 2 studies showing effectiveness, each with a p-value <0.05, were expected, that a single study could be adequate if the p-value was approximately 0.00125, and that providing evidence of durability of effect, as Study 303 was intended to provide, would be important." Ex. A at 4. Further, "[a]t a pre-IND meeting, the Division had previously advised the applicant that it would be important to assess efficacy over a longer period to demonstrate durability of effect. It is not clear why the sponsor did not power study 303 appropriately." *Id.* at 15. The memo repeated verbatim the language above in ¶90 regarding the deficiencies in the efficacy evidence and also stated that "[t]he data from site 507 seem highly irregular, and their reliability will have to be determined. If the data are ultimately deemed to be reliable, then study 301 could be considered positive, but for reasons explained above, it would not be sufficient to support an approval on its strength alone." Ex. A at 17. The memo concluded:

> ***We will issue a Complete Response action for this NDA, based on inadequate evidence of effectiveness***.
>
> Depending on the determination of reliability of the data from site 507 (study 301), ***I view the evidence of efficacy in this dossier to be either 3 negative studies, or 1 positive study (301) where 1 site is disproportionately responsible for the favorable effect, such that it alone does not provide a sufficient basis for approval.*** The concern about site 507 arose late in the review cycle, and

additional actions will be needed to address the data integrity questions.

> ***I strongly agree with the majority opinion on the review team that a demonstration of efficacy over a period of only 1 week is not adequate,*** given that patients with NOH have chronic disorders. This drug would surely be used on a chronic basis.

Ex. A at 19.

93. On the same day, Chelsea announced its receipt of the CRL from the FDA. In its press release, Chelsea stated that the FDA required an "additional positive Study to support efficacy . . . along with the recommendation that such a study be designed to demonstrate durability of effect over a 2- to 3-month period." Specifically, the press release stated in relevant part:

> The complete response letter includes the request by the FDA that Chelsea submit data from an additional positive study to support efficacy demonstrated in Study 301 along with the recommendation that such a study be designed to demonstrate durability of effect over a 2- to 3-month period. While the FDA did not make reference to the Company's ongoing Study 306, a 10-week double-blind, placebo-controlled trial evaluating Northera in patients with symptomatic neurogenic OH associated with Parkinson's disease, Chelsea believes that data from this trial could potentially meet the criteria for clinical efficacy and durability of effect data identified in the Complete Response Letter. Notably, the complete response letter did not identify any outstanding concerns. . . .
>
> Chelsea plans to request a meeting with the FDA to review the Agency's comments, clinical trial recommendations and to help determine appropriate next steps toward securing approval of Northera.
>
> "Chelsea is dedicated to improving the lives of patients with symptomatic Neurogenic OH," commented Dr. Simon Pedder, president and CEO of Chelsea Therapeutics. "We believe there continues to be an important unmet medical need in addressing the symptoms associated with Neurogenic OH and remain committed to working with the FDA to determine the appropriate next steps required to bring a much needed new therapy to the market as quickly as possible."

94. On this news, Chelsea common stock dropped $1.05 per share, or 28.7% to close on March 29, 2012 at $2.62 per share on unusually heavy volume.

95. Chelsea met with the FDA on May 2, 2012 to discuss the additional data and information required to resolve the outstanding items and deficiencies outlined in the CRL. *See* Ex. G at 2-3. During the meeting Chelsea and the FDA discussed the results from Site 507 and the FDA explained "the ease with which the investigational product could be unblinded, [] could have facilitated fraud (the contents of placebo and active capsules, although both white in color, are easily distinguishable; everyone associated with the study was aware that all subjects initially received the active drug)." Ex. G at 7. Chelsea agreed to submit all information pertaining to its investigation of site 507 to the FDA and to look into whether source data establishes that ***the enrolled subjects actually carried their stated diagnoses***. *Id.*

96. Shortly thereafter, on May 22, 2012, Chelsea issued a press release announcing its meeting with the FDA and disclosed for the first time that droxidopa patients at the highest enrolling center, Site 507, had a disproportionate contribution to the positive results of Study 301. *See* Press Release, Chelsea, Chelsea Therapeutics Completes End-of-Review Meeting with FDA for Northera™ (droxidopa) Capsules New Drug Application (2012). Chelsea stated in relevant part:

> As previously reported, the FDA's March 2012 CR Letter included the request by the FDA that Chelsea submit data from an additional positive study to support efficacy demonstrated in Study 301 along with the recommendation that such a study be designed to demonstrate durability of effect over a 2- to 3-month period. ***As noted in the CR Letter, FDA concerns related to one of the Study 301 clinical sites mitigated the persuasiveness of that study and prevented the FDA from accepting Study 301 alone as adequate evidence of effectiveness***. ***In contrast to the company's initial interpretation of the CR Letter, subsequent discussions with the FDA made it clear that issues related to the disproportionate contribution of a single center were of greater significance to FDA in issuing the CR Letter than were questions regarding durability of Northera's treatment effect.*** Significantly, the FDA was clear in acknowledging that aside from the results from the center in question, the review team takes no issue with results of Study 301, the favorable efficacy data for all US sites, favorable data for the secondary endpoints in Study 302, and positive blood pressure data in study 305.

97. On this news, Chelsea common stock dropped $0.25 per share, or 12% to close on May 22, 2012 at $1.84 per share on unusually heavy volume.

RELEVANT PRE-CLASS PERIOD STATEMENTS

98. On March 10, 2010, Chelsea filed its annual report for the fiscal year 2009 on Form 10-K with the SEC. Defendant Pedder signed the 2010 Form 10-K on behalf of the Company. The 2009 Form 10-K discussed droxidopa's clinical program, stating, in relevant part:

> ***In February 2008, we reached an agreement with the FDA on a Special Protocol Assessment, or SPA for the design of Study 301.*** The SPA process allows for FDA evaluation of a clinical trial protocol intended to form the primary basis of an efficacy claim in support of a NDA, and provides a binding agreement that the study design, including trial size, clinical endpoints and/or data analyses are acceptable to support regulatory approval. . . .
>
> ***In November 2009, we met with the FDA to review both the results of Study 302 as well as the results of an independent analysis of the sensitivity of efficacy scales used in Study 302***. ***As a result of this meeting, the FDA agreed to allow us to modify the primary endpoint and enroll an additional 24 patients in Study 301***, an on-going induction design, double-blind, placebo controlled pivotal Phase III study of droxidopa for the treatment of symptomatic NOH. . . .
>
> ***The FDA confirmed that while Study 302, which failed to achieve statistical significance using only item 1 of the OHSA as a primary endpoint, could not be used as a pivotal study, it did provide valuable information about the benefits of droxidopa. Both the safety and efficacy data from this study will be considered to be a supportive part of future regulatory filings***. Further, the FDA indicated that the number of patients already enrolled in our pivotal program would be sufficient to support the safety of droxidopa in an NDA in this indication.
>
> * * *
>
> ***In December 2009, we announced that after meeting with the FDA to obtain greater clarity about our options for completing the planned clinical and registration program for droxidopa, the FDA had agreed for us to change the primary endpoint and increase the enrollment of Study 301, our other ongoing pivotal Phase III trial, being conducted under a Special Protocol Assessment, or SPA.*** The primary endpoint of the trial will now be the relative improvement in the Orthostatic Hypotension Questionnaire (OHQ) composite score between droxidopa and placebo. The FDA agreed that the revised primary endpoint

> reflects a more comprehensive global assessment of the clinical benefit of droxidopa for the treatment of symptomatic NOH in primary autonomic failure, a heterogeneous population consisting of patients suffering from PD, MSA, PAF, Dopamine-ß-hydroxylase deficiency and non-diabetic autonomic neuropathy and would therefore be suitable for supporting a symptomatic claim. . . . ***The FDA subsequently confirmed that the SPA originally awarded to Study 301 in 2008 remained in effect following the protocol amendments approved by the FDA in December 2009.***
>
> ***The FDA also recommended that we submit a confirmatory pivotal study to support an NDA filing and that such study could be contained to a small, highly enriched, homogeneous patient population***. Based on this recommendation, we plan to initiate a new clinical trial, Study 306, in 2010. Study 306 is a randomized, double-blind, placebo-controlled, induction-design Phase III trial evaluating up to 84 patients with symptomatic NOH associated with PD.

99. Also on March 10, 2010, Defendants held a fourth quarter earnings conference call with investors and analysts. During the conference call Defendants stated in relevant part:

> [Analyst]: So, just a question regarding your partner – partnering strategy, droxidopa, so I think the cash is sufficient to – for release of one trial data, ***but presumably you need both trials to file, I guess at what point do you think partners will be interested in signing up with you, a deal***?
>
> [Pedder]: ***Obviously, we believed that everything that we've learnt has gone into the change that we've made and which the agency has blessed 301, and then gone into the design of 306.*** We in discussion with potential partners obviously identify what is the key data of events to make a decision, and obviously with the 302 initially been reported with negative views, but then coming back with very strong positive outcomes in many of the secondary parameters and the identification of OHQ as a very reliable composite score which does show benefit with pharmacological intervention with droxidopa has clearly made it 301 to be the key catalyst for companies to have discussions about entering into relationship with Chelsea, and clearly this is a competitive environment as we like to remind all those companies that we have those discussion with. . . .

100. On May 4, 2010, Chelsea filed its financial report for the first quarter of 2010 on Form 10-Q with the SEC ("1Q 2010 Form 10-Q"). The 1Q 2010 Form 10-Q discussed droxidopa's clinical program, stating, in relevant part:

> ***During the fourth quarter of 2009, we met with the FDA to obtain greater clarity about our options for completing the planned clinical and registration***

> ***program for Northera after the failure of Study 302. The FDA agreed for us to change the primary endpoint and increase the enrollment of Study 301, our other ongoing pivotal Phase III trial, being conducted under a Special Protocol Assessment, or SPA***. The primary endpoint of the trial is now the relative improvement in the Orthostatic Hypotension Questionnaire, or OHQ, composite score between Northera and placebo. The FDA agreed that the revised primary endpoint reflects a more comprehensive global assessment of the clinical benefit of Northera for the treatment of symptomatic NOH in primary autonomic failure, . . . and would therefore be suitable for supporting a symptomatic claim. . . .
>
> ***The FDA also recommended that we submit a confirmatory pivotal study to support a new drug application, or NDA, filing and that such study could be contained to a small, highly enriched, homogeneous patient population***. Based on this recommendation, we plan to initiate a new clinical trial, Study 306, in the second quarter of 2010.

101. On July 2, 2010, Chelsea filed a prospectus supplement on Form 424(b)(5) with the SEC. In regard to the clinical program for droxidopa, the prospectus supplement contained statements nearly identical to those in the 1Q 2010 Form 10-Q set forth in ¶100.

102. On July 27, 2010, Chelsea filed its financial report for the second quarter of 2010 on Form 10-Q with the SEC ("2Q 2010 Form 10-Q"). In regard to the clinical program for droxidopa, the 2Q 2010 Form 10-Q contained statements nearly identical to those in the 1Q 2010 Form 10-Q set forth in ¶100.

103. On the same day, Defendants held the second quarter 2010 earnings conference call with investors and analysts. During the conference call, defendant Schwieterman spoke deceptively about the strength of Chelsea's upcoming NDA for droxidopa, stating:

> [O]ur work to here and particularly this past quarter has resulted in some measurable achievements that collectively bode very well for the outcome of Study 301, ***achievements that should have us well positioned to file a strong NDA package***. And thinking about our experiences for 301 Study results, there are three key points that fuel our optimism for positive outcome.
>
> First, we have conducted extensive analyses of ***the results of Study 302 and have clear and unequivocal evidence of the efficacy of NORTHERA***, NOH. It was measured by a broad array of both symptomatic and functional assessment criteria. . . .

> ***We believe that the results in Studies 301 and 306 along with ancillary data from other safety studies will provide for a strong filing package***.
>
> And as we think about our filing strategy, we're fortunate to have a number of factors working in our favor. These include orphan designation, fast track status and the opportunity for enrolling submission, ***a very high probability of priority review for submission and a special protocol session for Study 301 that remain in effect and acceptable to the FDA***.
>
> ***All of this highlights, the very solid working relationship Chelsea has developed with FDA for this program***, add to this an extensive safety data base from the Japanese registration program and the substantial progress that has already been made to completing our CMC section and you can begin to appreciate the advantageous position we find ourselves in as we approach our NDA filing.

FALSE AND MISLEADING STATEMENTS DURING THE CLASS PERIOD

104. On September 20, 2010, the Company issued a press release announcing that the preliminary analyses of its Phase III droxidopa Study 301 met its primary endpoint. The Company stated the following, in relevant part:

> ***Chelsea Therapeutics International, Ltd. (NASDAQ: CHTP) announced that preliminary analyses of its Phase III NORTHERA™ Study 301 met its primary endpoint. Treatment with Northera provided clinically meaningful and statistically significant improvement (p=0.003) in symptoms associated with neurogenic orthostatic hypotension (NOH), a chronic and often debilitating drop in blood pressure upon standing.*** Study results also showed that Northera was both safe and very well tolerated.
>
> "We are extremely excited by these top-line results which provide validation of the safety and efficacy of Northera as a novel treatment for symptomatic neurogenic orthostatic hypotension, a serious condition for which there is an urgent need for improved treatments," said Dr. Simon Pedder, president and CEO of Chelsea Therapeutics. "Symptoms of chronic neurogenic orthostatic hypotension are severe, not only putting patients at high risk for falls and associated injuries but also severely impacting their quality of life and generating significant added health care costs. ***Northera is the first and only drug to repeatedly demonstrate clinical improvement in these patients by both alleviating symptoms of neurogenic orthostatic hypotension and improving their ability to perform daily activities."***

105. Defendants' statements in ¶104 above were materially false and misleading when

made because Defendants knowingly or recklessly failed to disclose that Chelsea had not disaggregated the results from Study 301 by country or site, obscuring the fact that without the highly unusual results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, Study 301's results were not statistically significant.

106. On December 20, 2010, Chelsea issued a press release announcing that it had completed a pre-NDA assessment with the FDA and intended to accelerate its NDA based on combined data from Chelsea's two completed Phase III studies in NOH, Study 301 and failed Study 302, without the need for any further efficacy studies. The press release disclosed that ***"[a]t the meeting, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from Chelsea's two completed Phase III studies in NOH, Study 301 and Study 302, without the need for any further efficacy studies***." Defendant Pedder further stated the following:

> ***The successful outcome of our pre-NDA meeting with the FDA reflects the strength of the data already generated by our pivotal program and marks a significant step forward for Chelsea.*** We believe that the Phase III trials we have already completed, combined with the extensive Japanese and European data available to us, clearly demonstrate Northera's meaningful clinical benefit to patients whose day to day lives are severely impacted by the signs and symptoms of neurogenic orthostatic hypotension.

107. During the conference call with investors and analysts held the same day to discuss the outcome of Chelsea's meeting with the FDA, Defendants echoed their misleading position on the strength of the Company's NDA, stating, in part:

> [Pedder]: The big news, of course, is that, ***based on the data presented, the FDA agreed with our proposal to file our NDA using Study 301 as a single pivotal study and Study 302 as supportive data***. As a result, the data from our currently ongoing comparative efficacy trial in Parkinson's disease patients, Study 306, will not be submitted as part of the clinical portion of the NDA, although these data will be provided to the FDA as supplementary information once the study is completed. . . .

While the Agency was clear that additional efficacy studies were not required for an NDA filing, they did express their interest in two additional studies, the first being a QTc study, and the second being a dedicated pharmacology study in renally impaired patients.

* * *

[Schwieterman]: ***We are very clear and explicit about the data we had from all of our studies. In fact, it was a fairly extensive briefing document we shared with the agency.***

We're very interested in being transparent about our data and highlighting not just the strengths of it, which are considerable, but also pointing out where there may have been issues that the FDA wanted to look into. We are very pleased because the whole point of the meeting was to get as much information as possible to make our NDA package as complete as possible. We are very pleased with their answers to all those questions. ***So I guess the short answer to your question is that they were presented with a very complete data set, and I think we are very well informed about everything.***

* * *

[Analyst]: Then with regards to the 306 data not being in the initial data package, the longest treatment duration you're going to have would be two weeks. Is there any -- do you expect any kind of change to the label because of the fact of the duration of treatment you have in the first two studies, or -- which should not be an impact?

[Pedder]: When it comes to the amount of time that they have been on, we have 165 patients treated for longer than one year. ***In our meetings with the Agency, they gave us a number of wanting about 100 patients treated per year, so we think that we have surpassed the request from the Agency to feel comfortable about the chronic safety of this compound***.

108. Defendants' statements in ¶¶106-107 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63 and 92

above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

109. On January 10, 2011, Chelsea filed a registration statement on Form S-3 with the SEC. In regard to the clinical program for droxidopa, the registration statement stated the following, in relevant part:

> ***In September 2010, we announced that upon preliminary analysis of Study 301, the second of our pivotal Phase III trials of Northera for the treatment of symptomatic NOH, the study had met its primary endpoint. Treatment with Northera provided clinically meaningful and statistically-significant improvement (p=0.003) in symptoms associated with NOH. Study results also showed that Northera was both safe and very well tolerated.*** Patients randomized into this double-blind, placebo-controlled study were evaluated for symptomatic and functional improvements using the orthostatic hypotension questionnaire, or OHQ, that is specifically designed to rate the severity of symptoms resulting from low-blood pressure and the degree to which those symptoms interfere with a patient's ability to perform activities of daily living. In addition to the symptomatic and functional benefits registered on the OHQ, the study validated Northera's unique mechanism of action and confirmed the preferential effect of Northera on standing systolic blood pressure, or SBP, versus supine SBP, demonstrating a statistically-significant improvement in standing SBP ($p<0.001$) relative to placebo. The study was conducted under a Special Protocol Assessment, or SPA, granted by the FDA in February 2008, providing an agreement that the study design, including trial size, clinical endpoints and/or data

analyses is acceptable to support regulatory approval. . . .

In December 2010, we completed a pre-NDA assessment meeting with the FDA. Based on the results of that meeting, we announced our intent to accelerate our planned new drug application, or NDA, for Northera for the treatment of NOH with an anticipated filing in the second quarter of 2011. During the meeting, the FDA agreed that our proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies in NOH, Study 301 and Study 302, without the need for any further efficacy studies as previous guidance had suggested. . . .

We had previously met with the FDA during the fourth quarter of 2009 after we announced in September 2009 the failure of Study 302, our initial pivotal Phase III trial, to meet its primary endpoint. At that meeting, the FDA agreed to a change in the primary endpoint and an increase in enrollment of Study 301, as they agreed that the revised primary endpoint reflected a more comprehensive global assessment of the clinical benefit of Northera for the treatment of symptomatic NOH in primary autonomic failure, a heterogeneous population consisting of patients suffering from Parkinson's disease, multiple systems atrophy, pure autonomic failure, dopamine-ß-hydroxylase deficiency and non-diabetic autonomic neuropathy, and would therefore be suitable for supporting a symptomatic claim. The FDA subsequently confirmed that the SPA originally awarded to Study 301 in 2008 remained in effect following the protocol amendments approved by the FDA in December 2009.

At that time, the FDA also recommended that we submit a confirmatory pivotal study to support our NDA filing and that such study could be contained to a small, highly-enriched, homogeneous patient population. Based on this recommendation, we initiated a new clinical trial, Study 306, in June of 2010.

110. Defendants' statements in ¶109 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its

primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

111. On February 2, 2011, the Company held a conference call with investors and analysts to discuss the droxidopa Phase III trial results. In regard to the NDA, Defendant Pedder stated:

> So moving on, what are the next steps for the Northera registration program? We are planning to file the initial Northera NDA submission in NOH third quarter of this year. ***It is still based on the efficacy data from the completed studies of 301 and 302 with obviously the safety data from the rest of our studies.***
>
> And just to remind you, we do have orphan status designation, we have fast track. We are anticipating a priority review. ***We are looking at approval of first quarter 2012 and launch Q2 2012***.
>
> * * *
>
> ***The pre-NDA meeting was regarding the adequacy of our dataset to show the safety and efficacy of droxidopa for the treatment of NOH. And they agreed that we have established that with 301 and 302***. . . .
>
> In fact, I would argue that actually we have added to the NDA to show that the OHQ now is supported by falls in this early study, and that by continuing to study that as the new objective that that will add added strength to the overall package and the overall program.

112. Defendant Schwieterman continued on:

> ***I mean the truth is every time we turn around we find better results than we expected. That happened with Study 301 where we had a P value of 0.003 allowing us then to go to the FDA and say we could file with 301 and 302. 306 was originally part of the plan to duplicate that trial but FDA found it unnecessary.***

113. Defendants' statements in ¶¶111-112 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63 and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

114. On February 17, 2011, Chelsea filed its preliminary prospectus supplement on Form 424(b)(5) with the SEC and the following day Chelsea filed the final prospectus

supplement. In regard to the clinical program for droxidopa, the prospectus said the following, in relevant part:

> We have previously completed two Phase III trials, Studies 301 and 302, of Northera for the treatment of symptomatic neurogenic orthostatic hypotension in patients with primary autonomic failure, a group of diseases including Parkinson's disease, multiple system atrophy and pure autonomic failure. ***The improvement in the symptoms of NOH as measured by the orthostatic hypotension questionnaire composite score, or OHQ composite, associated with Northera treatment in our pivotal efficacy Study 301 are highly significant (p<0.003)*** and showed similar improvements (p<0.05) in a post-hoc analysis of Study 302 data. ***On that basis, we proposed filing our NDA in symptomatic NOH. During our pre-NDA meeting in December of 2010, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies of Northera in NOH, Study 301 and Study 302 and their associated safety studies 303, 304 and 305, without the need for any further efficacy studies***. During the meeting, the FDA did request and we agreed to supply top-line results from a QTc study at the time of the 90-day safety update and conduct a post-marketing study to evaluate the clinical pharmacology of Northera in renally impaired patients.

115. Defendants' statements in ¶114 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided

evidence of the durability of Northera's effect; and

d) Chelsea did not break down the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

116. On March 2, 2011, Chelsea issued a press release announcing its fourth quarter and full year 2010 financial results. The press release summarized droxidopa's development milestones stating, in relevant part:

> ***Met primary endpoint, achieving highly significant improvement OHQ composite scores (p=0.003) in pivotal Phase III Northera Study 301*** in neurogenic orthostatic hypotension (NOH) . . .
>
> ***Reached agreement with FDA to file Northera new drug application (NDA) in symptomatic neurogenic orthostatic hypotension based on efficacy data from Studies 301 & 302***

117. On March 2, 2011, Chelsea also filed its annual report for the fiscal year 2010 on Form 10-K with the SEC ("2010 Form 10-K"). Defendant Pedder signed the 2010 Form 10-K on behalf of the Company. The 2010 Form 10-K discussed droxidopa's clinical program, stating, in relevant part:

> We have previously completed two Phase III trials, Studies 301 and 302, of Northera for the treatment of symptomatic NOH in patients with primary autonomic failure. ***The improvements in the symptoms of NOH, as measured by the orthostatic hypotension questionnaire composite score, or OHQ composite, associated with Northera treatment in our pivotal efficacy Study 301 are highly significant (p<0.003)*** and showed similar improvements (p<0.05) in a post-hoc analysis of Study 302 data***. On that basis, we proposed filing our NDA in symptomatic NOH. During our pre-NDA meeting in December of 2010, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies of Northera in NOH, Study 301 and Study 302, and their associated safety Studies 303, 304 and 305, without the need for additional efficacy studies.*** During the meeting, the FDA

did request and we agreed to supply top-line results from a QTc study at the time of the 90-day safety update. . . .

In September 2010, we announced that a preliminary analysis of Study 301 showed the study had met its primary endpoint. Treatment with Northera provided clinically-meaningful and statistically-significant improvement (p=0.003) in symptoms associated with NOH. Study results also showed that Northera was both safe and very well tolerated. The 167 patients randomized into this double-blind, placebo-controlled study were evaluated for symptomatic and functional improvements using the OHQ composite, which is specifically designed to rate the severity of symptoms resulting from low-blood pressure and the degree to which those symptoms interfere with a patient's ability to perform activities of daily living. In addition to the symptomatic and functional benefits registered on the OHQ composite, the study validated Northera's unique mechanism of action and confirmed the preferential effect of Northera on standing systolic blood pressure, or SBP, versus supine SBP, demonstrating a statistically significant improvement in standing SBP ($p<0.001$) relative to placebo. . . .

Given the highly significant outcome of Study 301, the FDA agreement that sufficient data exists to support an NDA filing without the results of Study 306 and given the outcome of the interim analysis, we now intend to modify Study 306 and use the data from this trial to form the basis for a future, supplemental claim of a reduction in falls associated with NOH in PD.

118. On the same day, Defendants held a fourth quarter earnings conference call with investors and analysts. During the conference call Defendants stated in relevant part:

[Schwieterman]: ***In this study, treatment with NORTHERA demonstrated a highly significant benefit over placebo in the OHQ composite score with a p=0.003. On a standalone basis, a p=0.003 serves as sufficient statistical power for a new drug approval***. ***This is not unique to Chelsea or to our NOH program. The FDA has often advised sponsors of one study with a p<0.001 that is considered persuasive for approval and p<0.01 could be acceptable if there is good internal consistency, low dropout rates with other supportive data*** in an area where there is a high unmet medical need. . . .

We have a remarkably strong filing package. In fact, in reviewing our proposed package, the only additional data requested by the agency was from the QTc study that we agreed to conduct and supply during the 90-day safety review.

* * *

[Analsyt]: So, two quick questions. One is for Bill, kind of the routine question about 0.03 versus 0.01 – 0.001. ***Just your confidence that 0.003, can it get you there with the single trial with the other studies as backup***. So, a 0.003

question and then a QT question to follow.

[Schwieterman]: Yeah. David, ***the answer is very confident***.

119. Defendants' statements in ¶¶116-118 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea did not break down the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

120. On April 6, 2011, Defendants attended the Needham & Company Healthcare Conference. During the conference Pedder stated, in relevant part:

> ***We had a meeting with the FDA, a pre-NDA meeting in December of last year, where they bought into the 301 and 302, our two Phase III studies, forming the***

basis of our filing. We have granted fast track status and we do anticipate priority review. ***Subsequently, by filing in third quarter of this year, we expect approval in the first quarter of 2012***.

121. Defendants' statements in ¶120 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

122. On April 18, 2011, the Company issued a press release confirming plans to file an NDA for droxidopa. The Company stated the following, in relevant part:

Following a comprehensive pre-NDA meeting with the FDA in December 2010 and subsequent communication with the agency, Chelsea plans to file its NDA

for Northera for the treatment of symptomatic NOH based on combined efficacy data from Chelsea's two completed Phase III studies in NOH, Study 301 and Study 302, during the third quarter of 2011. In keeping with the FDA's recommendations, Chelsea will not seek a falls claim in the initial labeling, but intends to continue its ongoing clinical evaluation of the effects of Northera in reducing the number of falls associated with NOH from Parkinson's disease and pursue future label expansion opportunities for Northera post-approval.

"***We believe the remarkable safety and tolerability of Northera coupled with the robust clinical benefit demonstrated throughout our Phase III program provide a strong basis for the approval of Northera as a novel treatment for symptomatic neurogenic orthostatic hypotension***," commented Dr. Simon Pedder, president and CEO of Chelsea Therapeutics. "***We continue to be appreciative of the guidance that the FDA has provided to Chelsea as we prepare to file this new NDA in the third quarter of 2011***. . . ."

123. Defendants' statements in ¶122 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in` its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site

507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

124. On May 2, 2011, during the Deutsche Bank Health Care Conference, Defendants again reiterated the false and misleading communications between the FDA and Chelsea regarding whether one trial would be sufficient for approval, stating:

> ***The basis of the filing will be the pivotal proof of efficacy study that was conducted under Special Protocol Assessment, or SPA, with the FDA. Study 301, which I'll quickly show you the data; as part of the 301 Study we also had a long-term safety to provide a long-term safety required by the agency*** and we also did 24 outlet pressure monitoring in a sub-group of patients that we call Study 305.
>
> * * *
>
> ***Well the meeting was held, the pre-NDA meeting was held in December and that's where we presented them significant amount of data***. . . . ***But that being said, the agency was very helpful in their discussions, telling us what they wanted to see in the filing. They did tell us that 301 would be suitable because the drug's orphan status and it's the biggest study that's ever been done in NOH***. ***And the highly statistical significance of the outcome was key for them in saying that we could file based on that***. . . . ***We were appreciative, they said it wouldn't be required for a filing but we would have to provide the three-month safety update. And so, we think they've been very supportive of the development program.***

125. Defendants' statements in ¶124 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its

primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54 above, and the fact that Study 301's results were not statistically significant without them.

126. On May 9, 2011, Chelsea filed its financial report for the first quarter of 2011 on Form 10-Q with the SEC ("1Q 2011 Form 10-Q"). The 1Q 2011 Form 10-Q discussed droxidopa's clinical program, stating, in relevant part:

> We have previously completed two Phase III trials, Studies 301 and 302, of Northera for the treatment of symptomatic neurogenic orthostatic hypotension in patients with primary autonomic failure, a group of diseases including Parkinson's disease, multiple system atrophy and pure autonomic failure. ***The improvements in the symptoms of NOH, as measured by the orthostatic hypotension questionnaire composite score, or OHQ composite, associated with Northera treatment in our pivotal efficacy Study 301 are highly significant (p<0.003)*** and showed similar improvements (p<0.05) in a post-hoc analysis of Study 302 data***. On that basis, we proposed filing our new drug application, or NDA, in symptomatic NOH. During our pre-NDA meeting in December 2010, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies of Northera in NOH, Study 301 and Study 302, and their associated safety Studies 303, 304 and 305, without the need for any further efficacy studies***. During the meeting, the FDA did request and we agreed to supply top-line results from a QTc study, which was initiated in the first quarter of 2011, at the time of the 90-day safety update and conduct a post-marketing study to evaluate the clinical pharmacology of Northera in renally-impaired patients.

127. On the same day, Defendants hosted a first quarter earnings conference call with

investors and analysts. During the conference call Defendant Schwieterman stated in relevant part:

> As we previously reported, the update was clear in our December pre-NDA meeting that the results of Study 306 would not be a required part of our submission. This position was subsequently reiterated in our communications with the agency following the interim analysis of Study 306 and the review of data from we now refer to as Study 306A.
>
> ***Therefore, based upon the FDA's guidance, it continues to be our intent to file our NDA based upon the robust and highly significant results of Study 301 including the results of Study 302 in support of efficacy data demonstrating the benefit of Northera treatment improving the signs and symptoms of neurogenic orthostatic hypotension***.

128. Defendants' statements in ¶¶126-127 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site

507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

129. On July 26, 2011, Defendants hosted a second quarter earnings conference call with investors and analysts. In regard to the clinical program for droxidopa, Defendants stated, in relevant part:

> [Schwieterman]: While this was certainly a significant event for us, it really isn't quite as interesting as the end product that is coming together as we continue our work with the NDA. Ultimately, ***as we get it further and further along in the process of assembling the NDA, I'm more and more impressed by the quality of our data and the strength of our filing package***.
>
> * * *
>
> [Analyst]: Can you again revisit why you guys are so confident that you could see the priority review? And again, as I speak to investors I get a lot of push back on the failed trial that we saw, the 302 study, and again, can you revisit what it is that is so strong about the 301 trial that gives you confidence in an approval? Thanks.
>
> [Schwieterman]: There's lots of reasons why we are confident about that, not the least of which is because we have already been designated fast track as part of our overall clinical development program. And programs that are on fast track generally get priority reviews just as part of that alone. But even irrespective of that, we have a drug that addresses a serious and unmet medical need. There are no proven established therapies out there that give patients symptomatic benefits for this condition. And we have shown multiple symptomatic benefits, as you know, through our OHQ and through other endpoints throughout the study. ***So the long and short of it is, is that the FDA has already granted us fast track. We've had discussions about priority review. They've given every indication that we're going to get that. And it's obvious that we have a therapy that's going to meet a serious and unmet medical need and in a big way. So we're quite confident.***
>
> [Analyst]: And again, the body language that you're getting from FDA with regard to getting this thing reviewed in a quick manner is saleable at this point?
>
> [Schwieterman]: Oh, yeah, yeah. ***We have had nothing but a good relationship with the FDA, and they've looked favorably on our data all throughout the program and that continues***. And we're very excited about the prospects, and as we've discussed, I think that this is going to get a quick review

at the Agency.

130. On the same day, Defendants filed a prospectus supplement on Form 424(b)(5) with the SEC. On the following day, July 27, 2011, Chelsea filed its financial report for the second quarter of 2011 on Form 10-Q with the SEC ("2Q 2011 Form 10-Q"). Both the prospectus supplement and the 2Q 2011 Form 10-Q contained statements nearly identical to those in the 1Q 2011 Form 10-Q set forth in ¶126.

131. Defendants' statements in ¶¶129-130 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant

without them.

132. On November 2, 2011, Chelsea filed its financial report for the third quarter of 2011 on Form 10-Q with the SEC ("3Q 2011 Form 10-Q"). The 3Q 2011 Form 10-Q discussed the clinical program for droxidopa stating, in relevant part, the following:

> The clinical portion of the NDA includes combined safety and efficacy data from our two completed Phase III studies in NOH, Study 301 and Study 302, two long-term open-label extension studies, Study 303 and Study 304, a dedicated thorough QTc study and a 24-hour ambulatory blood pressure monitoring study, Study 305. ***During our pre-NDA meeting with the FDA in December 2010 and in subsequent communication with the agency, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from these studies without the need for any further efficacy studies***.

133. Defendants' statements in ¶132 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site

507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

134. On November 17, 2011, Chelsea issued a press release announcing that the FDA accepted its NDA for droxidopa. In the press release Defendant Pedder represented that the Company was "confident that our Phase III data clearly establish the safety and efficacy of Northera for the treatment of the signs and symptoms of neurogenic orthostatic hypotension."

135. Defendants statements in ¶134 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54,

and the fact that Study 301's results were not statistically significant without them.

136. On January 5, 2012, Chelsea filed a preliminary prospectus supplement on Form 424(b)(3) with the SEC and the following day Chelsea filed a final prospectus supplement on Form 424(b)(5) with the SEC ("January 2012 Prospectus Supplements"). Both of the January 2012 Prospectus Supplements stated, in relevant part:

> The clinical portion of the NDA includes combined safety and efficacy data from our two completed Phase III studies in NOH, Study 301 and Study 302, two long-term open-label extension studies, Study 303 and Study 304, a dedicated thorough QTc study and a 24-hour ambulatory blood pressure monitoring study, Study 305. ***During our pre-NDA meeting with the FDA in December 2010 and in subsequent communication with the agency, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from these studies without the need for any further efficacy studies***. The FDA has also requested and we have agreed to conduct a post-marketing study to evaluate the clinical pharmacology of Northera in renally-impaired patients.

137. Defendants' statements in ¶136 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided

evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

138. On January 26, 2012, Chelsea filed a registration statement on Form S-3 with the SEC. The registration statement contained statements nearly identical to those in the January 2012 Prospectus Supplements set forth in ¶136 above.

139. Defendants' statements in ¶138 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or

site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

140. On February 13, 2012, Chelsea announced that the FDA had provided them with the FDA Briefing Document for the Advisory Committee Meeting. Specifically, Chelsea simply stated that "***several lines of inquiry . . . have emerged as significant components of the benefit-risk analysis of Northera***," and provided a summary of issues that had been "previously discussed":

> A number of these questions [in the FDA Briefing Document] relate to previously discussed issues identified for our development program, namely the short duration of our clinical studies, the limited size of our study population given the orphan indication and the challenges in quantifying symptomatic and clinical benefit. FDA has, however, placed increased emphasis on safety data from our long-term extension program and the post-marketing surveillance program in Japan. We look forward to the opportunity to address these questions in depth during the advisory committee meeting and to continuing to work with FDA to address any additional questions they may have regarding Northera and our clinical program.

141. Defendants' statements in ¶140 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the FDA Briefing Document's conlusion, namely, that "[o]n the basis of the safety concerns compounded by absence of evidence of durability of effect, my regulatory recommendation is that we should not grant approval for Droxidopa at this time."

142. On February 21, 2012, Chelsea issued a press release announcing the Advisory Committee Meeting on February 23, 2012. In the press release Defendant Pedder commented, "We have closely reviewed the materials prepared by the FDA, and look forward to presenting our clinical data to the Advisory Committee, which we believe will address ***the questions raised***

by the FDA," and "***We believe that our clinical program has established robust safety data and efficacy data for NORTHERA in this patient population***."

143. Defendants' statements in ¶142 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

144. On February 23, 2012, prior to the Advisory Committee Meeting, Chelsea released its Advisory Committee Briefing Materials ("Chelsea's Briefing Document"). Chelsea's Briefing Document stated, in relevant part:

Table 5-4 Results from the Hierarchy of Efficacy Endpoints (Study 301, Full Analysis Set with LOCF)

	Placebo (N=80)		Droxidopa (N=82)			
Efficacy Endpoints	n	Δ Mean (SD)	n	Δ Mean (SD)	Treatment Difference	p-value
Primary Efficacy Endpoint						
OHQ Composite Score	79	-0.93 (1.69)	81	-1.83 (2.07)	-0.9	0.003[1]
Secondary Efficacy Endpoints						
OHDAS Composite Score	79	-0.92 (1.82)	81	-1.98 (2.31)	-1.06	0.003[2]
OHSA Composite Score	79	-0.95 (1.90)	81	-1.68 (2.13)	-0.73	0.010[3]
OHDAS Item 1 (standing short time)	80	-0.8 (2.60)	82	-1.9 (2.75)	-1.1	0.003[2]
OHDAS Item 3 (walking short time)	80	-0.6 (2.37)	82	-1.7 (2.55)	-1.1	0.009[2]
OHSA Item 1 (dizziness)	80	-1.1 (2.58)	82	-2.4 (3.20)	-1.3	<0.001[3]
Improvement in the End of Study scores for the patient-rated CGI-S		–		–	–	0.327[4]

ANCOVA=Analysis of covariance; CGI-S= Clinical Global Impressions-Severity; Δ=Change; LOCF=Last observation carried forward; OHDAS=Orthostatic Hypotension Daily Activity Scale; OHQ=Orthostatic Hypotension Questionnaire; OHSA=Orthostatic Hypotension Symptoms Assessment; SD=Standard deviation.

Note: Efficacy endpoints are presented in hierarchical order.

1. The p-value from ANCOVA model included a factor for randomized treatment along with the OHQ composite value at Randomization as a covariate.
2. The p-value from non-parametric ANCOVA using Mantel-Haenszel statistics to compare treatment groups based on rank statistics adjusted for the covariate respective OHDAS Item score at Randomization. The OHDAS composite score used a parametric ANCOVA.
3. The p-value from the non-parametric ANCOVA using Mantel-Haenszel statistics to compare treatment groups based on rank statistics adjusted for the covariate respective OHSA Item score at Randomization. The OHSA composite score used a parametric ANCOVA.
4. The p-values were from Fisher's exact test comparing distribution of droxidopa responses to placebo responses at End of Study.

The results of the primary analysis from Study 301 showed that droxidopa provided patients with clinically meaningful and statistically significant benefits as measured by the mean change in the OHQ composite score (p=.003; Table 5-4). . . .

* * *

The data from Study 301 (Randomization to End of Study) demonstrate that droxidopa provides clinically meaningful and statistically significant benefits to patients with NOH as assessed by the OHQ composite score. In addition, more droxidopa-treated patients experienced improvements compared with placebo-treated patients across a range of OHQ improvement thresholds.

* * *

The pivotal efficacy study (Study 301) showed patients receiving droxidopa experienced broad and meaningful symptomatic benefits as measured by the OHQ composite score (0.9 unit mean change; p=0.003).

145. On February 23, 2012, during the Advisory Committee Meeting, Dr. Schwieterman presented an overview of the clinical development program for droxidopa, stating in relevant part:

Study 301 showed a statistically significant difference in favor of droxidopa on the mean change in the OHQ, the primary endpoint. Droxidopa patients had a numerical improvement of 1.83 in the OHQ composite score, as shown as a reduction on the Y axis, compared to a .93 reduction for placebo-treated patients. ***This .9 unit difference between treatment groups was associated with a p value of 0.003.*** . . .

The principal strength is that we demonstrated that droxidopa confers symptomatic benefit in randomized, placebo-controlled trials, including our largest randomized, controlled trial conducted under a special protocol assessment. ***Additionally, study 301 was a multi-center randomized, controlled study. Data were consistent across study subjects and sites, showed efficacy across multiple endpoints involving different events, and resulted in statistically very persuasive findings.*** These are all factors that are suggested by FDA to be considered when deciding if one successful trial is sufficient. . . .

When we approached the FDA, we asked them about the value of the 301 study, and we did not discuss that particular parameter. ***There was no set time when the FDA said it had to be below a particular p value,*** and that was consistent with our general understanding of the FDA's own guidance, where the use of p value is as a tool and so forth. ***So the answer to your question is there's nothing in our review with the agency; however, it was well understood that it would have to be quite low like p .003.***

146. On February 23, 2012, Chelsea held a conference call to discuss the results of the Advisory Committee Meeting with investors and analysts. During the conference call, Defendants projected extreme confidence regarding the NDA, stating, in relevant part:

[Analyst]: Thanks for taking my question. I know it's been a very long day for you. I guess the first thing that comes to mind is that the panel sort of unanimously suggested that you should do another trial to support approval and comments on maybe looking at longer duration of therapy . . .

[Pedder]: Well, first let me say that, I don't think everybody said that we needed another trial. I think everybody mentioned that they would like to see more data. And we're certainly interested in doing additional trials obviously through a post-marketing commitment. I find it a bit surprising, your comment, because ***we found the input of Dr. Stockbridge, Dr. Unger and Dr. Temple to be very helpful, especially in the discussions about why one clinical trial would, in fact, be appropriate in this indication***. . . .

[Analyst]: Okay. And on the color on the tone, you believe that the FDA was similar today to what they were in previous discussions.

[Pedder]: ***Very much, very much so***. I mean they don't agree with all of our comments or all of our discussion points, ***but certainly when it came to the interactive nature of the Agency, we've always had very fruitful discussions with them and I think that will continue***. . . .

[Schwieterman]: ***Yeah, thank you, Simon. No, I agree with your comments. I didn't feel like the tone of the FDA was any different than it's ever been with us***. . . .

[Schwieterman]: Yeah, Dr. Temple in particular had several comments to the meeting that I thought helped and formed the discussion and I was pleased about that. . . .

[Pedder]: Yeah, I mean I remember the time when we brought up back the – when people were talking about what was the size of the benefit that was meaningful, ***he in fact instructed for the 301 slide to be put up that looked at the OHQ and dizziness and showed the – that the large number of patients in fact have one unit when you look at two, three, four and even in fact more, you do see a pretty strong benefit of NORTHERA and he was instrumental on making sure that slide got back in front of the Advisory Committee members***.

* * *

[Analyst]: And again, I think one of the big questions is the P value of the 301 trial. They didn't come out and say it's sufficient, but certainly gave us enough information with regard to its sufficiency with the secondary out point.

[Pedder]: Well, thanks, thanks for that***. I will comment on one thing that doctor, I think it was Dr. Temple brought up, and that was not just about the P value, but all the supportive other symptoms and activities of daily living***. And Dr. Mark Stacy is here from Duke who presented some of that data. So, clearly the fact that everything was going in the right direction I think is one of the comments one of the advisors mentioned made him end up voting in the affirmative.

147. Defendants' statements in ¶¶144-146 above were materially false and misleading when made because Defendants knowingly or recklessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54, and the fact that Study 301's results were not statistically significant without them.

148. On March 7, 2012, Chelsea filed its annual report for the year ended 2011 on Form 10-K with the SEC ("2011 Form 10-K"). The 2011 Form 10-K discussed the clinical program for droxidopa, stating, in relevant part:

> We have previously completed two Phase III efficacy trials, Studies 301 and 302, of Northera for the treatment of symptomatic NOH in patients with primary autonomic failure. ***The improvements in the symptoms of NOH, as measured by the orthostatic hypotension questionnaire composite score, or OHQ composite, associated with Northera treatment in our pivotal efficacy Study 301 are highly significant (p<0.003)***. Northera showed similar improvements (p<0.05) in OHQ composite scores in a post-hoc analysis of Study 302 data. ***On that basis, we proposed filing our NDA in symptomatic NOH. During our pre-NDA meeting in December of 2010, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies of Northera in NOH, Study 301 and Study 302, and their associated safety Studies 303, 304 and 305, without the need for additional efficacy studies***. During the meeting, the FDA did request and we have supplied top-line results from a QTc study. . . .
>
> ***In September 2010, we announced that a preliminary analysis of Study 301***

showed the study had met its primary endpoint. Treatment with Northera provided clinically-meaningful and statistically-significant improvement (p=0.003) in symptoms associated with NOH. Study results also showed that Northera was both safe and very well tolerated. The 167 patients randomized into this double-blind, placebo-controlled study were evaluated for symptomatic and functional improvements using the OHQ composite, which is specifically designed to rate the severity of symptoms resulting from low-blood pressure and the degree to which those symptoms interfere with a patient's ability to perform activities of daily living. In addition to the symptomatic and functional benefits registered on the OHQ composite, the study validated Northera's unique mechanism of action and confirmed the preferential effect of Northera on standing systolic blood pressure, or SBP, versus supine SBP, demonstrating a statistically significant improvement in standing SBP ($p<0.001$) relative to placebo.

149. Defendants' statements in ¶148 above were materially false and misleading when made because Defendants knowingly or reckessly failed to disclose the following:

a) Since 2007 the FDA repeatedly recommended, as described in ¶¶43, 45, 47, 50, 57, and 63 above, that Chelsea submit an NDA with two pivotal studies demonstrating the efficacy of Northera (*i.e.*, with p-values of 0.05 or lower in each study's primary endpoint);

b) Since 2007 the FDA repeatedly stated, as described in ¶¶4, 42, 63, and 92 above, that a single study with a p-value of approximately 0.00125 in its primary endpoint "might" be acceptable under the FDCA's exception to the 2-study rule for a single multicenter study with exceptional results;

c) Since 2007 the FDA repeatedly recommended, as described in ¶¶42, 43, 45, 63, 64, and 73 above, that Chelsea submit an NDA that provided evidence of the durability of Northera's effect; and

d) Chelsea had not disaggregated the results from Study 301 by country or site for the FDA, obscuring the highly disproportionate results from Site 507 (State Medical Academy in Ukraine), as described above in ¶¶52-54,

and the fact that Study 301's results were not statistically significant without them.

150. None of the Class Period statements detailed above were ever corrected or updated by Defendants.

ADDITIONAL POST CLASS PERIOD EVENTS

151. On July 3, 2012, Chelsea announced that the FDA would not be accepting Chelsea's often-touted Study 306B as a supplement to the droxidopa NDA, based on the potential for "certain patients from Study 306B to have been unblinded in conjunction with the reporting of 306A data." According to an analyst research report issued on July 3, 2012 by Robyn Karnauskas and Navdeep Singh of Deutsche Bank, "[t]he FDA is taking a theoretical approach that Chelsea may have received hints of data from its CRL that would allow it to design the trial to work. The FDA has stated that Chelsea's 306B would not be adequate for approval due to this theoretical risk."

152. On November 7, 2012, Chelsea filed its financial report for the third quarter of 2012 on Form 10-Q with the SEC ("3Q 2012 Form 10-Q"). In regard to Study 306B, the 3Q 2012 Form 10-Q stated that "[s]oon after receipt of the written response from the FDA" Chelsea "stopped enrolling patients" in Study 306B and "modified the primary endpoint of Study 306B to the mean change in OHSA item #1 score (dizziness, lightheadedness, feeling faint or "feeling like you might black out") at visit 4 (one-week post titration)." Chelsea explained that "[r]esults from this study are expected by the end of 2012" and at that time it plans "to finalize and reach agreement with the FDA on an additional study design to fulfill the requirements for our planned resubmission of the Northera NDA."

153. On December 12, 2012, Chelsea announced in a press release that Study 306B

had met its revised primary endpoint, showing "that treatment with Northera provided clinically meaningful and statistically significant improvements compared to placebo in dizziness/lightheadedness at week 1 (1.0 unit change; p=0.018), the primary endpoint."

154. On February 20, 2013, the FDA issued guidance to Chelsea that Study 306B might support approval of droxidopa. More specifically, in a press release issued by Chelsea on that day, the Company explained that "it has received written guidance from the Director of the Office of New Drugs ('the Director') at the U.S. Food and Drug Administration (FDA) stating that Study 306B has the potential to serve as the basis for a resubmission of a Northera (droxidopa) New Drug Application (NDA) for the treatment of symptomatic neurogenic orthostatic hypotension (NOH)."

155. On July 9, 2013, Chelsea resubmitted its NDA for droxidopa with data from Study 306B. Shortly thereafter, on July 17, 2013, Chelsea announced in a press release that "[t]he FDA has deemed the resubmission a complete response to its March 28, 2012 Complete Response Letter and assigned a new Prescription Drug User Fee Act (PDUFA) goal date of January 3, 2014."

156. On February 18, 2014, Chelsea announced that the FDA granted accelerated approval for droxidopa stating, that the FDA "is approving Northera under the accelerated approval program, which allows for approval of a drug to treat a serious disease based on clinical data showing that the drug has an effect on an intermediate clinical measure (in this case, short-term relief of dizziness) that is reasonably likely to predict the outcome of ultimate interest (relief of dizziness during chronic treatment)." However, before it will grant full approval, the FDA is requiring Chelsea to conduct "a large, multi-center, placebo-controlled, randomized withdrawal study, which includes a 4-week randomized withdrawal phase preceded by a three

month open label run-in phase, designed with the goal of definitively establishing the durability of the clinical benefits of Northera[.]"

157. On May 8, 2014, Danish pharmaceutical company, Lundbeck, announced its plans to acquire Chelsea through a tender offer of all outstanding shares. *See* Press Release, Lundbeck AS, Lundbeck to Acquire Chelsea Therapeutics (May 8, 2014). The tender offer was closed on June 23, 2014. *See* Press Release, Lundbeck A/S, Lundbeck Successfully Completes Tender Offer for Chelsea Therapeutics (Jun. 23, 2014).

ADDITIONAL SCIENTER ALLEGATIONS

158. As alleged herein, Defendants acted with scienter because at the time that they issued public documents and made other public statements in Chelsea's name, they knew or recklessly disregarded the fact that such statements were materially false and misleading and/or omitted material facts concerning, among other things, the FDA's repeated requests that the NDA for droxidopa contain two successful studies demonstrating droxidopa's efficacy and one study showing durability of effect and that the "unusually aberrant" data from Site 507 was the sole reason Study 301 met its primary endpoint. *See, e.g., SEC v. Pirate Investor LLC*, 580 F.3d 233, 243 (4th Cir. 2009) ("[T]he fact that a defendant publishes statements when in possession of facts supporting that the statements are false is classic evidence of scienter."). Moreover, Defendants (i) knew that such documents and statements would be issued or disseminated to the investing public; (ii) knew that persons were likely to rely upon those misrepresentations and omissions; and (iii) knowingly and/or recklessly participated in the issuance and/or dissemination of such statements and/or documents as primary violators of the federal securities laws. Defendants' materially false and misleading statements and omissions of material facts artificially inflated Chelsea's stock price during the Class Period.

159. The Individual Defendants' scienter is further demonstrated by their senior-level positions at the Company which provided them with access to material, non-public information on a real-time basis concerning the meetings and communications with the FDA regarding the clinical program for droxidopa and the Study 301 data. For example, Defendant Pedder attended the August 21, 2007 meeting during which the FDA stated that two successful efficacy studies would be sufficient for approval (Ex. D at 2-3); Defendant Schwieterman attended the December 1, 2010 meeting during which the FDA reminded Chelsea that one efficacy study is not usually sufficient for approval and during which Chelsea failed to disclose to the FDA the nature of the results at Site 507 (Ex. H at 2-3); and both Individual Defendants attended the February 1, 2012 meeting during which the FDA expressed concern that the NDA did not show of durability of droxidopa's effect (Ex. K at 2-4). The exhibits attached hereto also show that the FDA held meetings with Chelsea on three other occasions, including when the study was ongoing, which were doubtlessly attended by at least one of the Individual Defendants. *See* Exs. A at 3, B at 20, C at 4. In regard to the results from Study 301, Chelsea chose to audit Site 507 on two occasions to ascertain whether the aberrant data was the result of fraud because it recognized the results appeared too good to be true. *See* Ex. F at 6. This would have been a decision for the Individual Defendants as top management.

160. Moreover, each of the Individual Defendants were highly educated, trained, and experienced in drug development, clinical trials, and the preparation and submission of licensing applications to the FDA. For example, Defendant Pedder received his Ph.D. in Pharmacology from the College of Medicine at the University of Saskatchewan in Canada. See Chelsea, Preliminary Revised Notice & Proxy Statement (Schedule 14A), 4 (Apr. 27, 2009). Pedder joined Chelsea in April 2004, and prior to that, from May 1994 to February 2003, Pedder was

employed by pharmaceutical giant, Hoffmann-La Roche. *See id.* In his nearly ten years at Hoffmann-La Roche, Pedder held various positions, including Director, Pharmaceutical Business, Pharmaceutical Development and Project Management, Vice President, Drug Development, and Vice President of Pharmaceutical Business, Oncology, and oversaw the development of the drugs Pegasys and Copegus which have combined annual world-wide sales of over $1 billion. *See id.* Defendant Schwieterman received his M.D. from the University of Cincinnati in 1980 and completed his internship and residency programs at Mt. Sinai Hospital in New York City in 1984. *See id.* Schwieterman worked for the FDA for many years and at one point served as Chief of the Medicine Branch and Chief of the Immunology and Infectious Disease Branch in the Division of Clinical Trials at the Food and Drug Administration. *See id.* From 2002 until Schwieterman was appointed as Chelsea's CMO in 2009, he worked as an independent consultant for pharmaceutical companies focusing on drug development and regulatory matters. *See id*.

161. As for Chelsea itself, the scienter of a corporation may be established through the scienter of the corporation's authorized agents. *See Matrix Capital Mgmt. Fund, L.P. v. BearingPoint, Inc.*, 576 F.3d 172, 182, 189-90 (4th Cir. 2009) (finding corporate scienter when "at least one corporate agent acted with the required state of mind" "even if the complaint does not name the corporate agent as an individual defendant or other-wise identify the agent."). Here, Pedder, Schwieterman, Hewitt, Szakas, Oliveto, and Rowse, all authorized agents of Chelsea, were present at meetings during which the FDA warned Chelsea that one study would not be sufficient for approval and that evidence of durability of effect would be important and during which Chelsea deceived the FDA by failing to disclose the data from Site 507. *See* Exs. C at 3 & 4, D at 1, H at 1, K at 2. An authorized agent of the Company also ordered and

conducted audits of Site 507 on two occasions. *See* Ex. F at 6. Accordingly, Chelsea acted with scienter while making contemporaneously false and misleading statements and omissions.

162. The Individual Defendants and Chelsea were further motivated to conceal Chelsea's tenuous chances of achieving FDA approval for Northera and the true extent of the concerns around the droxidopa clinical program because the Company was continuously reliant upon frequent securities offerings to the capital markets to implement its business strategy and planned product development efforts.

163. Up until the end of the Class Period, the Company had not received approval for the sale of any drug candidates in any market and, therefore, the Company had not generated any revenues therefrom. See Chelsea Therapeutics International, Ltd., Annual Report (Form 10-K), 22 (2011) (the "2011 Form 10-K"). The Company's business model during the Class Period thus was entirely dependent upon the successful development, regulatory approval and ultimate commercialization of Northera, Chelsea's most advanced investigational product candidate. *See id.*

164. As a development-stage company, Chelsea spent substantial cash in connection with implementing its planned product development efforts, clinical trials, commercialization and ultimate marketing activities for droxidopa. *See id.* at 39. With no source of income, Chelsea depended entirely on its ability to raise cash through various sources, such as equity and debt financing and the exercise of warrants or strategic alliances, to fund those operations during the Class Period. *See* 2011 Form 10-K at 22. Maintaining an inflated stock price was central to Chelsea's ability to attract the capital needed to fund the product development efforts, clinical trials, commercialization and ultimate marketing activities, as it allowed the Company to maximize each capital-raising opportunity.

165. During the course of its development program for Northera, Chelsea raised a total of $124.8 million through securities financing leveraged by the strength of the Company's inflated stock price. Starting in July 2009, Chelsea began raising substantial proceeds through the sale of common and preferred stock, various debt securities, and/or warrants to purchase any such securities in one or more offerings, often offered pursuant to prior shelf-registration statements filed with the SEC. Chelsea conducted the following offerings: (i) on July 28, 2009, the Company sold 3,325,000 shares of common stock at $4.00 per share pursuant to a shelf registration statement that became effective October 11, 2007, as amended pursuant to Rule 462(b), raising approximately $12.4 million net proceeds (*see* Press Release, Chelsea Therapeutics Completes $13.3 Million in Registered Direct Offering (July 29, 2009)); (ii) on March 5, 2010, the Company announced that it completed a registered direct offering to institutional investors for 6.7 million shares of common stock priced at $2.72 per share along with warrants to purchase approximately 2.3 million shares of its common stock, raising approximately $16.8 million net proceeds (see Press Release, Chelsea Therapeutics Completes $18.2 Million Registered Direct Offering (Mar. 5, 2010)); (iii) in July 2010, the Company filed the required documents and became eligible to use an at-the market common equity sales program for the sale of up to 3,000,000 shares of common stock pursuant to a shelf registration statement, effective August 20, 2009, and ultimately sold 634,500 shares of common stock under this program in September 2010, raising approximately $2.9 million net proceeds (see Press Release, Chelsea Therapeutics Announces Public Offering of Common Stock (Sept. 28, 2010)); (iv) in October 2010, Chelsea sold 8,214,286 shares of common stock at a price of $4.90 per share in a publicly-marketed offering pursuant to the August 20, 2009 registration statement, as amended pursuant to Rule 462(b), raising approximately $32.8 million net proceeds (*see* Press

Release, Chelsea Therapeutics Prices Public Offering of Common Stock (Oct. 1, 2010)); (v) in February 2011, the Company sold an additional 10,062,500 shares of common stock at a price of $4.00 per share in a publicly-marketed offering pursuant to a shelf registration statement, effective January 19, 2011, raising approximately $37.8 million net proceeds (*see* Press Release, Chelsea Therapeutics Prices Public Offering of Common Stock (Feb. 18, 2011)); and (vi) in January 2012, Chelsea sold 4,989,275 shares of common stock for $4.75 per share in a publicly-marketed offering pursuant to the January 19, 2011 shelf registration statement, as amended pursuant to Rule 462(b), raising approximately $22.1 million in net proceeds (*see* Press Release, Chelsea Therapeutics Announces Exercise of Over-Allotment Option and Completion of the Public Offering of Common Stock (Jan. 11, 2012)). With each of the above offerings, the Company explicitly stated its intention to utilize the net proceeds to fund its droxidopa programs, including the regulatory, commercialization, and marketing activities for Northera.

166. Chelsea desperately needed this cash because, as disclosed in its 2008 Form 10-K filed with the SEC on March 4, 2009, E&Y issued a going concern opinion based on the Company's incurred net losses and negative cash flows from operations during each period from inception through December 31, 2008. *See* Chelsea Therapeutics International, Ltd., Annual Report (Form 10-K), 51 (2009). E&Y noted that the Company had a deficit accumulated during the development stage of $69.8 million by December 31, 2008. *See id.* Chelsea itself admitted in its February 26, 2010 Prospectus Supplement that, absent the Company's continued ability to raise capital through securities offerings, it would not have been able to remain a going concern: "If we do not raise additional capital . . . the audit opinion we expect to receive from our independent auditors is expected to contain a notation related to our ability to continue as a going concern." *See* Chelsea Therapeutics International, Ltd., Prospectus Supplement (Form 424b5),

S-7 (2010).

167. However, with the cash from the collective offerings on hand throughout the Class Period, Chelsea was able to advance its investigational products, most notably the NDA for droxidopa. Indeed, Chelsea made no secret of the fact that the clinical development, FDA approval of droxidopa and ultimate commercialization of Northera was critically important to the Company's future. *See* 2011 Form 10-K at 22. Throughout the Class Period, Defendants and other representatives of the Company touted the commercial viability of Northera post-FDA approval, conditioning the investing public to view Chelsea's NDA for droxidopa as bound for approval, locking in promises of future streams of income.

168. In an effort to boost investor enthusiasm for droxidopa's "inevitable" FDA approval, Defendants frequently focused on the marketing potential for the drug. Defendants set the stage for their intention to market Northera as "the only drug that has ever shown to improve the symptoms of dizziness and lightheadedness," associated with NOH. Keith Schmidt, VP of Marketing and Sales, Chelsea Therapeutics International, Ltd., Chelsea Therapeutics at BioCentury's NewsMakers in the Biotech Industry Conference 4 (Oct. 22, 2010) (transcript available from Thompson Reuters) (the "October 22, 2010 Conference Call"). As Keith Schmidt (Chelsea's Vice President of Marketing and Sales) stated during the October 22, 2010 Conference Call, the potential market for the NOH population consists of between 170,000 and 180,000 patients, which he views as "a really sweet way to get into the market. It is a small enough market in terms of the sales force size we would need for the number of physicians we need to cover. And it is an easy way for us to commercialize – to get our Company ready to be a commercial organization." October 22, 2010 Conference Call Transcript at 6.

169. During the same conference call, Schmidt broke down the specific pricing

assumptions for the drug, determining that Northera would generate between "$300 million and $375 million in sales within three to five years." *Id.*

170. During the Class Period, Defendants continued to emphasize the critical importance of Northera to Chelsea and the drug's potential commercial viability. For example, during Chelsea's Q4 2010 Earnings Call, defendant Pedder stated:

> [A]s an orphan status drug, we are very happy that this is a drug whereby we are not talking about a tumor type where there is only 40,000 patients and they may get three cycles and then unfortunately they regress. This is a population in the United States we think maybe excess of 150,000 and our idea is when we get them on drug, we'll keep them on drug for a very long period of time chronically. That's how it's used in Japan, so that's certainly how we expect it to be used here in the U.S. and the other areas that we have as it is in Japan. But what has happened with the interesting data albeit in small numbers is people are kind of tying into the fact that if you do prevent people from having orthostatic hypotension, if you do stop them from getting dizzy, you may in fact stop them from falling, which has a huge healthcare cost in this country and globally. And subsequently to that, they see perhaps increased demand for the use of this drug, and clearly what we have done albeit with small numbers is show a dramatic effect in the biggest population that have NOH which is Parkinson disease patients. And so it's probable that some companies are looking at this drug with a little bit more homerun potential than they did the first time they looked at it. But it certainly doesn't change the way that we have always looked at it. This is a drug that is going to help the population that it's going to treat and it's not just the fact of stopping them from feeling dizzy, it's going to give them better quality of life.

171. Focusing attention on the marketability of the drug diverted the investing public's attention away from droxidopa's insufficient clinical trials and the overall weaknesses in droxidopa's NDA.

CLASS ACTION ALLEGATIONS

172. Lead Plaintiff brings this action pursuant to Rule 23(a) and 23(b)(3) of the Federal Rules of Civil Procedure on behalf of himself and a putative class consisting of all persons and entities that purchased or otherwise acquired publicly traded Chelsea common stock in the United States or on the NASDAQ Stock Market during the Class Period at artificially inflated

prices and who suffered damages as a result (the "Class"). Excluded from the Class are the Defendants named herein, members of their immediate families, any firm, trust, partnership, corporation, officer, director or other individual or entity in which a Defendant has a controlling interest or which is related to or affiliated with any of the Defendants, and the legal representatives, heirs, successors-in-interest or assigns of such excluded persons. Also excluded are those investors who purchased stock during the Class Period but sold the shares prior to the corrective disclosures set forth herein.

173. The members of the Class are so numerous that joinder of all members is impracticable. While the exact number of Class members is unknown to Lead Plaintiff at this time and can only be ascertained through appropriate discovery, Lead Plaintiff believes that there are thousands of members in the proposed class. Throughout the Class Period, Chelsea common shares were actively traded on the NASDAQ. As of January 20, 2012, Chelsea had more than 67 million shares of common stock outstanding. Record owners and other members of the Class may be identified from records maintained by Chelsea or its transfer agent and may be notified of the pendency of this action by mail, using the form of notice similar to that customarily used in securities class actions.

174. Lead Plaintiff's claims are typical of the other members of the Class because Lead Plaintiff and all of the Class members sustained damages that arose out of the Defendants' unlawful conduct complained of herein.

175. Lead Plaintiff will fairly and adequately protect the interests of the members of the Class, and Lead Plaintiff has no interests that are contrary to, or in conflict with, the interests of the Class members that he seeks to represent. Lead Plaintiff has retained competent counsel experienced in class action litigation under the federal securities laws to ensure such protection

and intends to prosecute this action vigorously.

176. The prosecution of separate actions by individual Class members would create a risk of inconsistent and varying adjudications, which could establish incompatible standards of conduct for Defendants. Questions of law and fact common to members of the Class predominate over any questions that may affect only individual members in that Defendants have acted on grounds generally applicable to the entire Class. The questions of law and fact common to the Class include, but are not limited to, the following:

a) whether Defendants' acts violated the federal securities laws as alleged herein;

b) whether Defendants' publicly disseminated statements during the Class Period omitted and/or misrepresented material facts;

c) whether Defendants acted with scienter in omitting and/or misrepresenting material facts;

d) whether the price of Chelsea common stock was artificially inflated during the Class Period as a result of the material misrepresentations and omissions complained of herein;

e) whether the Individual Defendants were controlling persons as alleged herein; and

f) whether members of the Class have sustained damages and, if so, the proper measure of such damages.

177. A class action is superior to other methods for the fair and efficient adjudication of this controversy since joinder of all members of the Class is impracticable. Furthermore, as the damages suffered by individual members of the Class may be relatively small, the expense

and burden of individual litigation make it impossible for members of the Class to individually seek redress for wrongs done to them. There will be no difficulty in the management of this action as a class action.

LOSS CAUSATION

178. During the Class Period, as detailed herein, Defendants engaged in a scheme to deceive the market and a course of conduct that artificially inflated Chelsea's stock price and operated as a fraud or deceit on Class Period purchasers of Chelsea stock by misrepresenting the Company's business and prospects. During the Class Period, Defendants misrepresented and concealed the true facts regarding the Company's communications with the FDA, the strength of the NDA, and the disproportionate results contributed by Site 507 to Study 301. Later, however, as Defendants' prior misrepresentations, omissions, and scheme were disclosed and became apparent to the market, the price of Chelsea stock fell precipitously. As a result of his purchases of Chelsea stock during the Class Period at artificially inflated prices, Lead Plaintiff and other Class Members suffered damages as the truth was revealed.

179. Defendants' wrongful conduct, as alleged herein, directly and proximately caused the damages suffered by Lead Plaintiff and the Class. Defendants' false and misleading statements and omissions in their SEC filings and other public statements during the Class Period directly caused losses to Lead Plaintiff and the Class. On the strength of these statements, the Company's stock price was artificially inflated to a Class Period high of USD $8.15 per share on January 10, 2011. Those misrepresentations and omissions that were not immediately followed by an upward movement in the Company's stock price served to maintain the share price at artificially inflated levels by maintaining and supporting a false positive perception of Chelsea's business, operations, performance, and prospects.

180. As the truth began to emerge regarding the true nature of droxidopa's NDA and the FDA's communications with Chelsea, the price of Chelsea's stock declined as the market processed each set of previously undisclosed facts. Each such disclosure removed a portion of the artificial inflation in the price of Chelsea's common stock and directly and proximately caused Lead Plaintiff and other Class members to suffer damages. For example, on February 13, 2012, when Chelsea announced *inter alia* receipt of the FDA Briefing Document and that "several lines of inquiry . . . have emerged as significant components of the benefit-risk analysis of Northera," Chelsea's shares declined $1.88 per share, or more than 37.5%, to close at $3.11 per share. Similarly, following the publication of the FDA Briefing Document containing scathing criticism of Chelsea's NDA and recommending that droxidopa should not be approved due to, *inter alia*, the "absence of durability of effect," Chelsea common stock dropped approximately 21% to close at $2.64 per share on February 21, 2012. Chelsea's common stock declined an additional 28% on heavy trading volume after the Company disclosed in a press release on March 28, 2012 that it had received the CRL where the FDA rejected the NDA for droxidopa, closing at $2.62 per share on March 29, 2012. Finally, on May 22, 2012, after Chelsea disclosed the disproportionate results from Site 507, Chelsea common stock dropped $0.25 per share, or 12% to close at $1.84 per share on unusually heavy volume.

181. Until shortly before Lead Plaintiff filed this Complaint, he was unaware of the facts alleged herein and could not have reasonably discovered Defendants' misrepresentations and omissions by the exercise of reasonable diligence.

CONTROL PERSON LIABILITY

182. The Individual Defendants are liable as direct participants with respect to the wrongs complained of herein. In addition, the Individual Defendants, by reason of their status as

senior executive officers and/or directors, were "controlling persons" within the meaning of Section 20(a) of the Exchange Act, and each had the power and influence to cause the Company to engage in the unlawful conduct complained of herein. Because of their positions of control, the Individual Defendants were able to and did, directly or indirectly, control the conduct of Chelsea's business.

183. Specifically, because of their positions within the Company, the Individual Defendants possessed the power and authority to control the contents of Chelsea's annual and quarterly reports, press releases, and presentations to the FDA, the Advisory Committee, securities analysts, money and portfolio managers, and institutional investors, *i.e.*, the market, including those containing the materially false and misleading statements and omissions of material fact alleged herein. Each of the Individual Defendants, by reason of his respective management or board position, had the ability and opportunity to review copies of the Company's SEC filings, reports, press releases, and other public statements alleged herein to be false and misleading, prior to, or shortly after their issuance or to cause them to be corrected.

184. By virtue of their positions, the Individual Defendants had access to material nonpublic information. Each of the Individual Defendants knew or recklessly disregarded the fact that the adverse facts specified herein had not been disclosed and were being concealed from the public, and that the positive representations which were being made were then materially false and misleading.

THE FRAUD ON THE MARKET PRESUMPTION

185. At all relevant times, the market for Chelsea's publicly traded stock was an efficient market for the following reasons, among others:

a) Chelsea's common stock was listed and actively traded on the NASDAQ

(symbol CHTP), a highly efficient national market;

b) As a registered and regulated issuer of securities, Chelsea filed periodic reports with the SEC, in addition to the frequent voluntary dissemination of information;

c) Chelsea regularly communicated with public investors through established market communication mechanisms, including through regular dissemination of press releases on the national circuits of major newswire services and through other wide-ranging public disclosures such as communications with the financial press and other similar reporting services;

d) The market reacted to public information disseminated by Chelsea;

e) Multiple analysts followed Chelsea's business and wrote reports which were publicly available and affected the public marketplace;

f) The material misrepresentations and omissions alleged herein would tend to induce a reasonable investor to overvalue Chelsea's stock; and

g) Without knowledge of the misrepresented or omitted facts, Plaintiff and other members of the Class purchased or otherwise acquired publicly traded Chelsea stock between the time Defendants made material misrepresentations and omissions and the time that the truth was revealed, during which time the price of Chelsea stock was artificially inflated by Defendants' misrepresentations and omissions.

186. As a result of the above, the market for Chelsea common stock promptly digested current information with respect to the Company from all publicly available sources and

reflected such information in the security's price. The historical daily trading prices and volumes of Chelsea publicly traded stock are incorporated herein by reference. Under these circumstances, all purchasers of Chelsea common stock during the Class Period suffered similar injuries through their purchases of shares at prices which were artificially inflated by Defendants' misrepresentations and omissions. Thus, a presumption of reliance applies.

THE AFFILIATED UTE PRESUMPTION

187. At all relevant times, Lead Plaintiff reasonably relied upon Defendants to disclose material information as required by law and in the Company's SEC filings. Lead Plaintiff would not have purchased or otherwise acquired Chelsea common stock at artificially inflated prices if Defendants had disclosed all material information as required. Thus, to the extent Defendants wrongfully failed to disclose material facts and information concerning the approval of droxidopa by the FDA, or otherwise omitted material facts and information, Lead Plaintiff is presumed to rely on Defendants' omissions as established by the Supreme Court in *Affiliated Ute Citizens v. U.S.*, 406 U.S. 128 (1972).

NO STATUTORY SAFE HARBOR

188. As alleged herein, Defendants acted with scienter because, at the time that they issued public documents and other statements in Chelsea's name, they knew that such statements were materially false and misleading or omitted material fact. Moreover, Defendants knew that such documents and statements would be issued or disseminated to the investing public; knew that persons were likely to rely upon those misrepresentations and omissions; and knowingly participated in the issuance and/or dissemination of such statements and/or documents as primary violators of the federal securities laws.

189. As set forth in detail in the Complaint, the Individual Defendants, by virtue of

their control over, and/or receipt of Chelsea's materially false and misleading statements and/or their association with the Company which made them privy to confidential proprietary information concerning Chelsea which was used to artificially inflate financial results and which the Individual Defendants caused or were informed of, participated in and knew of the fraudulent scheme alleged herein. With respect to non-forward looking statements and/or omissions, the Individual Defendants knew and/or recklessly disregarded the false and misleading nature of that information that they caused to be disseminated to the investing public.

190. The statutory safe harbor provided for forward-looking statements under certain circumstances does not apply to any of the allegedly false or misleading statements pleaded in this Complaint. Many of the specific statements pleaded herein were not identified as "forward-looking statements" when made and/or were statements of historical fact. Rather, the statements alleged herein to be false and misleading all relate to facts and conditions existing at the time the statements were made. Moreover, meaningful statements did not identify important factors that could cause actual results to differ materially from those in any putative forward-looking statement.

191. Alternatively, to the extent that the statutory safe harbor does apply to any forward-looking statements pleaded herein, Defendants are liable for those false forward-looking statements because at the time each of those forward-looking statements was made, the particular speaker knew that the particular forward-looking statement was false or misleading, and/or the forward-looking statement was authorized and/or approved by an executive officer of Chelsea who knew that those statements were false or misleading when made. None of the historic or present tense statements made by Defendants were an assumption underlying or relating to any plan, projection, or statement of future economic performance, as they were not stated to be such

an assumption underlying or relating to any projection or statement of future economic performance when made nor were any of the projections or forecasts made by Defendants expressly related to or state to be dependent on those historic or present tense statements when made.

CAUSES OF ACTION

COUNT I

For Violations of Section 10(b) of the Exchange Act and Rule 10b-5 Against All Defendants

192. Lead Plaintiff re-alleges each allegation above as if fully set forth herein.

193. This claim is brought under Section 10(b) of the Exchange Act, 15 U.S.C. §78j(b) and Rule 10b-5 promulgated thereunder by the SEC, 17 C.F.R. § 240.10b-5, against Chelsea and the Individual Defendants.

194. During the Class Period, Defendants violated Section 10(b) of the Exchange Act and Rule 10b-5(b) promulgated thereunder by disseminating and/or approving the false and misleading statements specified herein, including statements in SEC filings, presentations, and press releases, on conference calls, and statements to the FDA and the Advisory Committee concerning the Company's NDA for droxidopa, Chelsea's study results, Chelsea's communications with the FDA, and the likelihood the FDA would approve the application, whose truth they knowingly or recklessly disregarded when they failed to disclose material facts necessary to make the statements made, in light of the circumstances under which they were made, not false and misleading.

195. During the Class Period, Defendants violated Section 10(b) of the Exchange Act and Rule 10b-5(a) & (c) promulgated thereunder by employing devices, schemes, and artifices to defraud and engaging in acts, practices, and a course of conduct that operated as a fraud or deceit

upon Plaintiffs and other members of the Class in that Defendants concealed the disproportionate results from Site 507 from the FDA, the Advisory Committee, and the investing public.

196. Defendants, individually and in concert, directly and indirectly, by the use, means or instrumentalities of interstate commerce and/or the mails, engaged and participated in a continuous course of conduct that operated as a fraud and deceit upon Lead Plaintiff and the Class; made various false and/or misleading statements of material facts and omitted to state material facts necessary to make their statements made, in light of the circumstances under which they were made, not misleading; made the above statements with a severely reckless disregard for the truth; and employed devices and artifices to defraud in connection with the purchase or sale of securities, which were intended to, and did (i) deceive the investing public, including Lead Plaintiff and the Class, regarding, among other things, Chelsea's communications with the FDA, the strength of the Company's NDA for droxidopa, the significance of Study 301 in light of the disproportionate results from Site 507, and the likelihood that the FDA would approve Chelsea's NDA; (ii) artificially inflate and maintain the market price of Chelsea common stock; and (iii) cause Lead Plaintiff and other members of the Class to purchase Chelsea common stock at artificially inflated prices.

197. Defendant Chelsea is liable for the false and misleading statements made by its officers in press releases, during conference calls, and at conferences with investors and analysts, and for the acts, practices, and course of conduct employed by its officers and agents that operated as a fraud or deceit, as alleged above, under the principle of respondeat superior. The Individual Defendants, as top executive officers and/or directors of the Company, are liable as direct participants in the wrongs complained of herein. Through their positions of control and authority as officers of the Company, each of the Individual Defendants was able to and did

control the content of the communications with the FDA and the public statements disseminated by Chelsea. The Individual Defendants had direct involvement in the daily business of the Company and participated in the preparation and dissemination of Chelsea's false and misleading statements in addition to Chelsea's fraudulent scheme, as set forth above.

198. As described above, Defendants acted with scienter throughout the Class Period in that their conduct was undertaken knowingly and intentionally, or in such an extremely reckless manner as to constitute willful deceit and fraud upon Lead Plaintiff and other members of the Class who purchased Chelsea stock during the Class Period.

199. Lead Plaintiff and the Class purchased Chelsea common stock without knowing that Defendants had misstated or omitted material facts about, *inter alia*, Chelsea's communications with the FDA, the strength of the NDA for droxidopa, and the significance of Study 301 in light of the disproportionate results from Site 507. Lead Plaintiff and the Class would not have purchased Chelsea common stock at the prices they paid, or at all, if they had been aware that the market price had been artificially and fraudulently inflated by Defendants' false and misleading statements and deceptive devices and acts. In purchasing the stock, Lead Plaintiff and the Class relied directly or indirectly on false and misleading statements made by Defendants, and/or an absence of material adverse information that was known to Defendants or recklessly disregarded by them but not disclosed in Defendants' public statements. Lead Plaintiff and the Class were damaged as a result of their reliance on Defendants' false and misleading statements and omissions of material facts.

200. Lead Plaintiff and the Class are filing this action within two years after discovery of the facts constituting the violation, including facts establishing scienter and other elements of Plaintiff's claim, and within five years after the violations with respect to the investments of the

Lead Plaintiff and the Class.

201. By virtue of the foregoing, Defendants have violated § 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder.

202. As a direct and proximate result of Defendants' wrongful conduct, statements, and omissions, Lead Plaintiff and the other members of the Class suffered damages in connection with their purchases of Chelsea common stock during the Class Period.

COUNT II

For Violations of Section 20(a) of the Exchange Act Against the Individual Defendants

203. Lead Plaintiff re-alleges each allegation above as if fully set forth herein.

204. This Count is asserted against Defendants Pedder and Schwieterman, the Individual Defendants, for violations of Section 20(a) of the Exchange Act, 15 U.S.C. § 78t(a), on behalf of all members of the Class.

205. As alleged in detail above, Chelsea committed a primary violation of Section 10(b) of the Exchange Act by knowingly and/or recklessly disseminating materially false and misleading statements and/or omissions throughout the Class Period as well as by participating in a scheme to conceal the aberrant results from Site 507 from the FDA, the Advisory Committee, and the investing public.

206. During their tenures as officers and/or directors of Chelsea, each of the Individual Defendants was a controlling person of Chelsea within the meaning of Section 20(a) of the Exchange Act. By reason of their positions of control and authority as officers and/or directors of Chelsea, these Defendants had the power and authority to cause Chelsea not to engage in the wrongful conduct complained of herein. As set forth in detail above, the Individual Defendants named in this Count were able to and did control, directly and indirectly, and exert control over

Chelsea, including the content of the public statements made by Chelsea during the Class Period, thereby causing the dissemination of the false and misleading statements and omissions of material facts as alleged herein. Therefore, the Individual Defendants are jointly and severally liable for the Company's fraud, as alleged herein.

207. In their capacities as senior corporate officers of Chelsea, and as more fully described above, the Individual Defendants had direct involvement in the day-to-day operations of the Company and in its financial reporting functions as well as Chelsea's communications with the FDA and the Advisory Committee. Each of the Individual Defendants was also directly involved in providing false or misleading information and signing and/or approving the false or misleading statements disseminated by Chelsea during the Class Period. Further, as described above, the Individual Defendants had direct involvement in the presentation and/or manipulation of false or misleading reports included within the Company's press releases and statements to the SEC, the FDA, and the Advisory Committee. Thus, the Individual Defendants knew or recklessly disregarded the fact that Chelsea's representations were materially false and misleading and/or omitted material facts when made. In so doing, the Individual Defendants did not act in good faith.

208. As alleged in detail above, the Individual Defendants controlled and managed Chelsea's overall business and controlled and/or possessed the authority to control the contents of the Company's reports, press releases, and presentations to securities analysts and, through them, to the investing public.

209. By reason of their positions as officers of Chelsea, and more specifically as controlling officers—as can be seen by their corresponding ability to influence and control Chelsea—each of the Individual Defendants is a "controlling person" within the meaning of

Section 20(a) of the Exchange Act and had the power and influence to direct the management and activities of the Company and its employees, and to cause the Company to engage in the unlawful conduct complained of herein. Because of their positions, the Individual Defendants had access to adverse nonpublic financial information about the Company and acted to conceal the same, or knowingly or recklessly authorized and approved the concealment of the same. Moreover, each of the Individual Defendants was also involved in providing false information and certifying and/or approving the false and misleading statements disseminated by Chelsea during the Class Period. Each of the Individual Defendants was provided with or had access to copies of Chelsea's reports, press releases, public filings, and other statements alleged by Lead Plaintiff and the Class to be misleading prior to and/or shortly after these statements were issued and the ability to prevent the issuance of the statements or cause the statements to be corrected.

210. By virtue of their positions as controlling persons of Chelsea and as a result of their own aforementioned conduct, the Individual Defendants named in this Count are liable pursuant to Section 20(a) of the Exchange Act, jointly and severally with, and to the same extent as the Company is liable under Section 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder, to Lead Plaintiff and the other members of the Class who purchased or otherwise acquired Chelsea common stock. Moreover, as detailed above, during the Class Period the Individual Defendants served as officers of Chelsea and each of these Defendants is culpable for the material misstatements and omissions made by Chelsea, including such misstatements in the Company's press releases, Forms 8-K, 10-K, and 10-Q.

211. As a direct and proximate result of the Individual Defendants' conduct, Lead Plaintiff and the other members of the Class suffered damages in connection with their purchase or acquisition of Chelsea stock.

PRAYER FOR RELIEF

WHEREFORE, Lead Plaintiff on behalf of himself and the Class, prays for relief and judgment including:

A. Determining that Counts I and II of this action are a proper class action under Rule 23 of the Federal Rule of Civil Procedure, certifying Lead Plaintiff as Class representative under Rule 23 of the Federal Rules of Civil Procedure, and certifying Lead Plaintiff's counsel as Class Counsel;

B. Awarding compensatory damages in favor of Lead Plaintiff and the other Class members against all Defendants, jointly and severally, for all damages sustained as a result of Defendants' wrongdoing, in an amount to be determined at trial, including pre-judgment and post-judgment interest, as allowed by law;

C. Awarding extraordinary, equitable and/or injunctive relief as permitted by law (including, but not limited to, rescission);

D. Awarding Lead Plaintiff and the Class their costs and expenses incurred in this action, including reasonable counsel fees and expert fees; and

E. Awarding such other and further relief as may be just and proper.

JURY TRIAL DEMANDED

Lead Plaintiff hereby demands a trial by jury on all triable claims.

Dated: July 8, 2015

Respectfully submitted,

By: */s/ Richard W. Gonnello*

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CERTIFICATE OF SERVICE

I hereby certify that on July 8, 2015, I authorized the electronic filing of the foregoing with the Clerk of the Court using the CM/ECF system which will send notification of such filing to the e-mail address denoted on the attached Electronic Mail Notice List, and I hereby certify that I caused to be mailed the foregoing document or paper via the United States Postal Service to the non-CM/ECF participants indicated on the attached Manual Notice List.

By: */s/ Richard W. Gonnello*
Richard Gonnello